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THE MEDICAL CLINICS
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VOLUME 2 NUMBER 4

CLINIC OF DR. S. W. BANDLER

POST-GRADUATE HOSPITAL

STERILITY IN WOMEN, WITH ESPECIAL REFERENCE TO ENDOCRINE TREATMENT OF THE SAME

Pituitrin in Obstetrics. Why is Gynecology Becoming More Medical? Facts from Practical Experience which Tend to Prove the Value of Endocrine Therapy.

January 24, 1919.

THE topic this morning is sterility in women. As the endocrines bear such an important relation to this question it is essential to spend a few moments discussing the physiology of the endocrines before coming to the main subject.

Most of you have heard me speak of some of these points before in connection with numerous clinical cases, and so you will have to take the old with the new. On the chart shown on page 922 is a short outline which we will use as an introduction to the subject of the endocrines as they concern the gynecologist and the obstettrician.

The human body is managed by the endocrine glands of the body. You have an automobile, and it is run by gasoline of one kind. In spite of the fact that it has a competent mechanism, if you are short of gasoline or have a poor quality of gasoline, that invalidates the value of the automobile. But in the human body you have many kinds of gasoline given off by many glands, each gland producing many secretory elements. The particular division of these secretions we do not yet understand, but

CHART No. I

Development: Pelvis — Chlorosis — Anomalies of menstruation — Neurotic symptoms—Tachycardias.

Ovary, Thyroid, Pituitary } Menstruation (a crisis): Amenorrhea—Relative Amenorrhea—Dysmenorrhea—(Marriage).

Premenstrual phenomena: { Congenital, Acquired } Thirteen times a year upset.

Pregnancy (amenorrhea): Toxemia—generally slight—Severe type. Action of corpus luteum.

Labor (a crisis): Pituitrin—Forceps.

Postpartum asthenia: Lactation atrophy—often starvation or *gland exhaustion.*

(Mammary Extract):

Sterility: Curet?

Repeated abortion: Wassermann.

Hyperthyroidism: Interglandular upset — Reflex — Hysteria(?) — Neurasthenia(?).

Menopause: Flushes { Excited, Depressed } Psychoses.

Postpartum psychoses: Puerperal mania.

Dementia præcox.

each gland and its special components has definite specific action, and every individual from the time he is born until the time he dies is under the influence of these many different kinds of elements—some of them having to do with the development of the bones and teeth, some with the development of the body and nervous system, some with the development of the mind, etc., and, later on—with the introduction of the sex factors—with reproduction. Still later on these elements have to do with the preservation of these structures and functions which constitute the body and mind; and if the gasoline elements which are given off by these glands become under- or overactive you have a disturbance of the specific functions these component parts are supposed to perform, and as these glands are dependent upon each other the upset of one disturbs the rhythmic action of the others; so that a woman during her development and maturity keeps in action as her glands keep in normal action, and as she approaches the climacterium and, later on, the years of senility, her glands change and her activities change; so that

if she lives long enough she is pretty nearly back to where her body function started in the early years.

We must not forget that the pituitary and thyroid have much to do with the development of the body and bones, as may be seen from cretinism. The development of infantilism is traced in many cases to the lack of proper developmental stimuli by the thyroid or pituitary glands. The development of the status lymphaticus shows the importance of the thymus and its associated lymphatic activities. The thymus is supposed to decrease at a time when the gonadal function develops. Hence, among its functions is supposed to be that of inhibiting a too early development of the sex glands. Now, we have a different body development in the male and in the female, and we explain that by the fact that the secretions of the testes so act on the other glands of the body, especially the anterior pituitary and adrenal cortex, as to increase their activity and give a heavier bony framework, larger hands, and larger stature; while the ovaries, not affecting the other glands to the same extent, are accompanied by a lesser stimulation of the anterior lobe of the pituitary and other glands controlling the development of bone, and the result is a smaller stature, smaller hands, etc. Hence the difference in shape and character of the male and female pelvis. *The anterior lobe of the pituitary acts more specifically in the male than in the female; the posterior acts more characteristically in the female than in the male.*

Consider for a moment the question of chlorosis, which is observed exclusively in the girl after the establishment of puberty, and you will see that the etiology of this blood state has been referred to a weak spot in the blood-forming function in which the ovary is supposed to play a part. Therefore many of these cases have been benefited by the administration of ovarian extract. Others have been markedly benefited by ovarian extract to which are added iron and arsenic. As a result I have adopted the rule that when I want to increase the activity of the ovarian extract I frequently add iron and arsenic; and I usually add ovarian extract to iron and arsenic when given for any form of anemia unless the patient is suffering from menorrhagia, in which

case the ovarian extract is omitted and an endocrine extract, such as mammary or thymus or anterior pituitary, which diminish menstruation, is added.

We now come to the stage of puberty, the time when the girl first menstruates, and in your experience you will notice numerous anomalies of menstruation: that which comes on slowly or late; that which comes on at irregular periods, during any of which you may have slight or great degrees of tachycardia; you will observe many cases of menorrhagia; or you will note major or minor forms of neurotic symptoms, so that many of these girls have to be taken out of school. They are nervous and irritable, on edge, cannot concentrate, cannot do their work, and many are filled with peculiar thoughts and obsessions, not infrequently taking on a sexual character. These anomalies of menstruation, these tachycardias, these psychic symptoms are due to the fact that the ovary, in asserting itself as a new and powerful member of the endocrine family, upsets the other members and relationships, until finally, in the vast majority of cases, harmony is established. If it is established easily and quickly, the girl menstruates regularly and there are no annoying symptoms. If harmony be established slowly and with difficulty, you have more of the above-mentioned annoyances. If no permanent smooth action is established, you have a condition where every menstruation acts badly on the system, so that we must speak not only of dysmenorrhea in the old accepted meaning of the term, but instead speak of *constitutional dysmenorrhea*. It is the same as when a man marries; sometimes the new wife fits into the new family relationships with harmony, sometimes not; and just as these families react differently to the introduction of the new member, so the endocrines react to the introduction of the ovarian element.

What do these neurotic symptoms at this developmental stage mean to us?

They mean that hundreds of girls have, from fifteen to nineteen or twenty years of age, various forms of physical and psychic phenomena which, though they smooth themselves out in the vast majority of cases, and eventually allow the possessors

to become normal, suggest at the time *minor* forms of those psychoses which are not so rare during the developmental age. Dementia præcox, as you know, is a condition affecting the growing boy or girl at the developmental age. It is in many instances an hereditary condition, and in the large majority of cases it is incurable. What can be made responsible for this condition except an interglandular upset? What makes such a boy or girl develop in a fairly normal way up to a certain stage and then show abnormality, eventually leading on to a well-defined form of dementia præcox?

These various points are suggestions, but they mean that every girl or boy is a potential dementia præcox. Practically every person is a potential manic-depressive. We all have our periods of elation and of depression, with cause and without cause, but our endocrine relationship preserves a tolerable balance; but if this endocrine upset is pronounced and manifests its activity or its influence mainly on the nervous system, you may have a developmental psychosis. This can be explained on no other basis than endocrine instability and endocrine upset.

Take the example of postpartum mania, where the patient goes out of her mind. What does that mean? That individual may have been perfectly normal all her life. As a result of having a baby, she develops a mania from which she may recover or may not. The trouble does not originate in the brain, which has acted normally all her life; but some gland crisis or glandular anomaly resulting from the introduction and subsequent removal of the placental secretion has so disturbed her cerebral activity that she is like one poisoned by an infectious disease. These cases, however, usually recover. There is, because of some change in the endocrine relationship, a toxic or irritating action on certain brain centers or functions.

We now come to menstruation, a period in which the ovary, pituitary, and thyroid are concerned. At every menstruation these three act or react, and according to the harmonious action of the three you have either a normal menstruation or menorrhagia, a relative amenorrhea, or varying degrees of actual amenorrhea.

Now, the glands which preside especially over menstruation are the ovaries. Without ovaries no menstruation takes place. The ovaries are more or less under the domination of other glands of the body. The thyroid has an important part in preserving and aiding the normal action of the ovary and uterus. The pituitary gland is intimately connected with the genital apparatus. As you know, an affection of the posterior lobe of the pituitary gland, whereby its secretion is diminished, is associated with progressive gain in weight, and a progressive diminution of menstruation, and an eventual greater or lesser degree of atrophy of the uterus and ovaries. On the other hand, if the secretion of the posterior lobe be increased, we have the opposite condition, excessive menstruation and the development of fibromata and myomata, and the so-called fibrosis uteri.

Now in every menstruation the thyroid reacts to the menstrual stimulus and the posterior lobe of the pituitary undoubtedly plays its part. If the posterior lobe of the pituitary reacts excessively during the menstrual stimulus initiated by the ovary, we get a dysmenorrhea; and I believe that many of the dysmenorrheas are due to excessive action of the posterior pituitary lobe during this monthly crisis. Nothing shows the nerve reaction of a patient more than the way she suffers physically or mentally or nervously before menstruation comes on.

Before each monthly crisis the ovarian secretion produces a gradually increasing congestion or hyperemia in the endometrium; but with this is associated a hyperemia of most of the mucous membranes of the body. The mucous membrane of the nose, the larynx, the gastric mucosa, etc., take part in this general hyperemia a week or ten days before menstruation. The thyroid and the posterior lobe react to this ovarian stimulation; hence a patient's interglandular relation is upset in many cases. Gynecologists have an advantage in this respect, that by taking a thorough history of the premenstrual and menstrual phenomena of patients, we have a very, very important index as to the patient's glandular or interglandular stability. Many patients are made aware by no definite symptoms whatsoever that menstruation is coming on. Others feel a fulness in the breasts or a

pain or discomfort in the pelvic region; others have marked discomfort a few days before menstruation; many women are very irritable or are depressed in this premenstrual stage. Some are irritable almost to the degree of slight mania; others cry and show bursts of temper; others have varying degrees of unusual sexual or psychic manifestation. Some have decided headaches, with or without nausea or vomiting. Such an experience reproduced every month not only indicates lack of nerve resistance to these premenstrual stimuli, but profoundly affects the patient more or less disagreeably and more or less permanently.

The manner in which a patient reacts to the premenstrual stage gives me a most valuable index, and I do not doubt its meaning. It is to be expected that in those patients whose glands do not act harmoniously at this period we may take for granted a latent instability of the interglandular relationship; and if you watch your patients closely at the premenstrual phase you will then see them show baby or minor forms of psychic disturbances which markedly suggest the psychoses which we speak of, when of the major type, as dementia præcox or manic-depressive insanity, or the various forms of mania and mental aberration.

To conclude this part of the discussion, we may say the less a patient suffers constitutionally before every menstruation, the more normal her menstruation is in amount and character; the less pain she suffers during menstruation, the more normal we may consider that individual's endocrine system. Every menorrhagia, every metrorrhagia, every relative amenorrhea, every greater degree of actual amenorrhea must first be considered from the standpoint of the endocrines. Of course there are many other causes of menorrhagia and metrorrhagia, but these, in turn, must be diagnosed according to the bimanual findings and according to the history.

Why is pregnancy characterized by amenorrhea?

When the fecundated ovum settles in the intra-uterine lining it nests and embeds in the decidua. As it grows, the outer layer of the ovum, which is called the trophoblast, invades the surrounding tissue and digests it by an enzyme action. Cells

from the trophoblast are given off immediately into the circulation, and this giving off continues as the ovum grows and chorionic villi develop and as the subsequent placenta comes into being. This secretion produced by the outer layer of cells and the subsequent chorionic villi and the subsequent placenta has the power to nullify the menstrual stimulus initiated by the ovary and aided by the thyroid and the pituitary. During the entire period of pregnancy the ovaries, the thyroid, the pituitary, the adrenals, and other protective glands of the body are fighting against that new secretion introduced by the growing ovum.

The next evidence of the trophoblast secretion which we have is the nausea and vomiting that pregnant patients complain of. If the protective glands adapt themselves to this new substance, the nausea and vomiting are slight. If they do not adapt themselves readily or quickly, then the nausea and vomiting are more pronounced, and later on in the pregnancy we have the various degrees of toxemia and finally eclampsia—all of which are undoubtedly due to the fact that protective glands do not give these patients the immunity which the vast majority of patients do gain in the course of a few weeks.

When a child develops scarlet fever or diphtheria it is because the adrenals or the pituitary gland, etc., of that child no not render it immune. A weak protective glandular resistance is an invitation to infection. Not long ago I delivered a patient, and on that corridor another patient, an adult, developed diphtheria. What was to be done? Of course we removed the baby from the corridor, and the first thing which we did was to make the Schick test, and as the baby proved to be immune we had no further worry so far as the child was concerned. Why is one child shown to be immune by this test and another child not? This is explained only on the basis of interglandular relationship in the one case which gives immunity, and a lack of that sufficient power in the next child which does not grant immunity. The same holds good in the present epidemic of influenza and influenza pneumonia. It seems to attack persons in the prime of life, in the period when the gonad apparatus is supposedly most active. The epidemic is not so severe in children where the gonad-

apparatus is not so developed, nor in older people where the gonadal apparatus has disappeared as a functionating process.

Influenza, especially the severe cases, represents a systemic infection, and the poison seems to have a predilection for the uterine mucosa, and many pregnant patients stain or miscarry, and many patients instead of going to full term have a premature labor. Many patients who are not pregnant, within a week after the infection, have an increased menstruation, anticipating the normal one by several days. It must be remembered that the uterine lining is a lymphoid tissue, with the exception of its glands and epithelial cells, resembling the tonsils. The toxic cases in the present epidemic of influenza represent probably an invasion past the lymphoid and lymphatic system when the thymicolymphatic system and the chromaffin systems fail to give sufficient protection. After invasion of the system, the subsequent course shows that the glands whose function it is to take care of the genital tract are especially affected by the toxin developed by influenza. When a pregnant patient, especially one near full term, is attacked by this pneumonia epidemic her interglandular apparatus (pituitary, adrenal, etc.), already weakened by fighting against placental aggression, is especially liable to injury, and the power of resistance granted by these glands is naturally less than in the normal individual.

Now just a few words about the use of corpus luteum, by mouth or by hypodermic, for the nausea and vomiting of pregnancy. Theoretically speaking, it ought to be very valuable to us, since true corpus luteum is only formed when pregnancy takes place. However, one cannot rely on it as a specific. It may help in some cases, but in routine use it has failed to have any definite value. The average person recovers with mild medication, or after the use of the Murphy drip (2 per cent. sod. bicarb., 5 per cent. glucose) for a week or two for the nausea and vomiting of pregnancy, and goes on in a perfectly normal manner.

On the other hand, pregnancy does have a remarkably stimulating effect on many patients, and it is no infrequent thing to see a slightly built girl develop wonderfully with excel-

lent color and increase in her hemoglobin, increase in the size of her bones, as the result of pregnancy. The anterior pituitary, the adrenal cortex, and the thyroid are stimulated and act well. The matter is rather different in the postpartum stage. Some patients are characterized by evidences of glandular exhaustion, which is intensified in many patients by nursing, especially if prolonged. If prolonged, we have the condition known as lactation atrophy, in which menstruation has been inhibited during nursing by the action of the mammary extract. The act of nursing separates from the mammary glands certain substances which have an inhibiting and restraining influence on the ovaries, posterior pituitary, and uterus, leading to an atrophy or subinvolution. There may be a marked constitutional effect associated with this prolonged nursing, the evidence then being a marked deficiency of the stimulating secretory glands of the body, such as the ovary, thyroid, and especially the pituitary and the adrenals. It is not very difficult to restore menstruation due to lactation atrophy by the administration of ovarian extract plus thyroid extract. The element of exhaustion or asthenia is of importance, and in these cases we add suprarenal extract and pituitary extract, *whole* gland, for its general tonic effect. Some patients have many children, even in rapid succession, and are perfectly well and in nowise exhausted. Some women after one baby suffer exhaustion which, while it may improve, is more or less permanent. In other words, certain individuals are potential asthenics, and pregnancy and labor add the final blow; and they practically never recover from the effect of the drain which has been put on their protective glands by the invasion of the system by the placental secretion.

As a general proposition, it may be stated that a nursing mother who menstruates has an endocrine system less readily held in check than has the mother who is characterized by amenorrhea during lactation. From this physiologic fact we deduce that mammary extract ought to be of value in many forms of menorrhagia due to ovarian pituitary or uterine causes, and experience proves this deduction to be correct.

What is labor?

Labor is a crisis, and in that crisis certain glands—particularly the ovary, thyroid, and pituitary, which normally are concerned in menstruation and which have been inhibited by the trophoblast and placental secretions—again come into action, with the result that on the two hundred and eightieth day you have a menstruation which did not take place during the duration of pregnancy. Something occurs which brings ovary, thyroid, and pituitary back into their old function. The inhibiting element is gone. Now, menstruation is a miniature labor. The processes of dilatation of the cervix, expulsion of non-fecundated ovum, loss of blood, are miniature reproductions of the various processes which occur in labor. Therefore we have pituitrin acting when the patient is in labor, whereas it does not act until the crisis occurs. If given when the patient is in labor, it increases the pains, adds to their force, and its action is generally all that can be desired. Some inhibitory element has disappeared or some sensitizing element has come into being. If you give pituitrin before the patient is in labor, or before her expected time, it may bring on labor-pains, but in the large majority of instances it has no further effect.

Why does it act when given by hypodermic during labor or at the time the patient is supposed to go in labor, and not at an earlier date? Because labor is a crisis, and you will find that pituitrin, given in proper doses and at proper intervals during labor at a time when forceps seem to be indicated, almost entirely displaces the need of forceps.

Now, we come to the question of repeated, habitual miscarriage. We have laid much stress on the meaning of the Wassermann test in this type of patient, but there are any number of cases of habitual miscarriage in which the Wassermann test is negative. Where formerly I used thyroid extract plus arsenic, plus bichlorid of mercury, plus stypticin for months to carry a patient to full term, I now find the results even better by relying almost entirely on endocrine treatment—giving the patient the trophic support which she needs and increasing the resistance to those factors which tend to produce miscarriage.

What is the cause of repeated miscarriages?

The ovary, thyroid, and pituitary are trying each month to produce menstruation; the placenta is trying for two hundred and eighty days to inhibit it. If the ovary, thyroid, and pituitary, especially the pituitary, are not too energetic, the placental element nullifies the menstrual tendency, holds it up for two hundred and eighty days, until labor ensues at the expected time. If the placental element cannot inhibit this tendency to menstruation, you have a menstruation early in pregnancy, which is a miscarriage, at two months, three months, four months, etc.; so the whole is a matter of when the crisis occurs. If it occurs at the expected time, you have a full-term pregnancy; if it occurs earlier, you have a miscarriage, or premature labor.

So we give to these patients the secretions which have a tonic influence and a trophic effect; we give no pituitary extract in any form, for we fear the too early evidence of the action of that gland. We give mainly ovarian extract, corpus luteum, and thyroid.

Now we know that in hyperthyroidism patients may be improved by the administration of pituitary extract. If the reverse be the case and you have hyperpituitarism, you may oppose the specific action on the pregnant uterus by the administration of thyroid; so that the administration of the latter extract in repeated miscarriages may be explained by this trophic action and by its opposing the excessive and too early sensitized introduction of the pituitary element.

The introduction of pituitrin into obstetrics has marked a momentous advance. Labor-pains and the actual force which the uterus is exerting in expelling the fetus are two different things. A patient may have little pain, and progress may be normal; she may have no pains at all, worthy of the name—uterine inertia; she may have very severe pains, with no progress. The use of pituitrin in 3-minim doses, with the pelvic measurements normal and the head engaged firmly in and through the brim, and well molded, will deliver the vast majority of babies without the use of forceps. Obstetrics has

been too little surgical in its trend; gynecology has been too surgical.

We turn to cesarean section as an example. In those cases where the test of labor aided by pituitrin shows no molding and no engagement of the head in and through the brim, we do this rather than apply the forceps on such a head. The indication for cesarean section is even more clear when the head does not engage at all, but bobs above the brim. In placenta prævia with a viable child, cesarean section has every advantage, in that it saves the baby and is far less dangerous for the mother. When dealing with a clean case handled under sterile precautions, even if examined, cesarean section, in my opinion, is to be preferred to the use of high forceps. So, with the introduction of this surgical element into obstetrics and with the introduction of the use of pituitrin, we find forceps less and less indicated.

Why is gynecology getting to be less surgical?

Simply because we understand our patients better and pay less and less attention to the element of reflex. The day when a lacerated cervix, or a slight cystocele, or a retroversion, are considered by reflex changes to be the cause for many women's nervous symptoms I believe to be past. Gynecology has abandoned this explanation for nervousness and nervous symptoms, just as movable kidney is no longer made to bear the burden for innumerable general phenomena. If the kidney is extremely movable, if the patient suffers from Dietl's crises, if we are sure that it is responsible for the pain of which the patient complains, that kidney should be fixed; but we know that movable kidney is present in so many women who have had children, and that in those and other cases it is part of a general abdominal ptosis, or part of a congenital or acquired asthenia, that we no longer expect by an operation on the kidney to correct symptoms of a systemic or nerve nature. We see many women with lacerated cervices who complain of general nervous states; we see innumerable others who have had no children at all who evidence the same symptoms. Why should we operate on one and consider it responsible for the patient's general annoyances, when the next patient has the same general annoyances without the

lacerated cervix? And this criticism holds good for many of the minor gynecologic conditions on which operations have been done so recklessly in the past. We must remember that lacerated feelings are much more responsible for nervousness than a lacerated cervix or perineum can be.

We now explain these so-called cases of hysteria and neurasthenia, and the innumerable and various nervous phenomena with which women suffer, on the very practical theory of glandular upset; and among these upsets hyperthyroidism, so frequent in women, proves to be the most frequent. The relation of ovarian secretion—altered by changes in the circulation, by slight degrees of inflammation, by the development of the so-called cystic ovary—to upset in the glandular action is only too clear. Changed ovarian secretion may be the cause of glandular upset; and altered ovarian secretion (glandular upset) is often the result of pituitary or thyroid abnormalities, even to the degree of anatomic cystic changes in the ovaries themselves.

Then we come to the menopause state, with the types varying from the depressed to the excitable, and to the combination of these two states. All of these are now to be explained by interglandular changes and alterations which occur in every woman at the climacterium. If these changes develop harmoniously, the patient has a placid menopause. If the new relationship established between the glands by the diminishing function of the ovary and the coincident diminishing function of the thyroid, pituitary, and other glands is not established easily and harmoniously, we have hyperthyroidism, hypothyroidism, hyperpituitarism, hypopituitarism, and innumerable combinations involving these glands as well as the suprarenal, pancreatic, and other structures. That many cases of glycosuria are the result of the interglandular changes, and that an excess of pituitary action likewise is responsible for many cases of glycosuria and fibroid uterus seems more than probable.

Now I will devote the rest of this talk to the subject of sterility.

Figure 174 shows the uterus in normal position with a moderate degree of anteflexion. It shows the posterior fornix, which

is supposed to represent a pouch or culdesac into which the seminal fluid is deposited, so that the cervix by dipping into it gives easy opportunity for the ingress of the spermatozoa. Some have considered one of the causes of sterility to be an anomaly whereby there is an angle instead of a pouch at the posterior fornix. On the theory that the seminal fluid runs out readily they have considered this anomaly to be one of the causes of sterility, and have treated these cases by successive packings of the vagina with gauze, and in that way believe they have developed a culdesac. So far as my observations have gone I have not found this to be a matter of any great importance.

Fig. 174.—The spermatozoa are deposited in the posterior fornix.

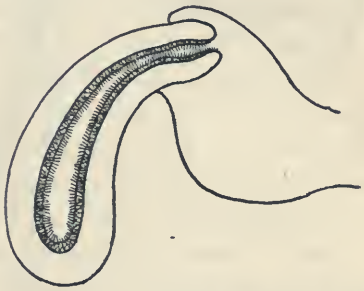

Fig. 175.—With retroflexion the cervix is not in contact with the reservoir formed by the posterior fornix.

Then comes the question of retroflexion (Fig. 175). If you are dealing with a retroflexion, as has been depicted above, with the cervix pointing horizontally or upward, you have naturally less opportunity for the spermatozoa to be in continuous contact with the cervix, and many men have considered and do consider retroflexion a frequent cause of sterility. It is, of course, the correct idea to replace every retroflexed uterus with the aid of a pessary. The trouble is that most congenital retroflexions cannot be restored to the normal position by this means. The cervix is high up and nearer the symphysis than is normal because the anterior wall of the vagina and the uterovesical ligaments are congenitally

short. To replace the retroflexed uterus it is essential that the cervix should be pushed high up and far back in the direction of the hollow of the sacrum. If then the fundus fall forward, as it naturally will if movable and not held by adhesions, the proper pessary by holding the cervix in this natural position mechanically corrects the retroflexion.

The next chart brings us to the question of inflammation (Fig. 176). You may have inflammation of the cervix with or without a very thick plug of yellowish, greenish, mucoid secretion; you may have the inflammation affecting the lining of the uterus, the cornual or interstitial area of the tubes, the entire lumen of the tube,

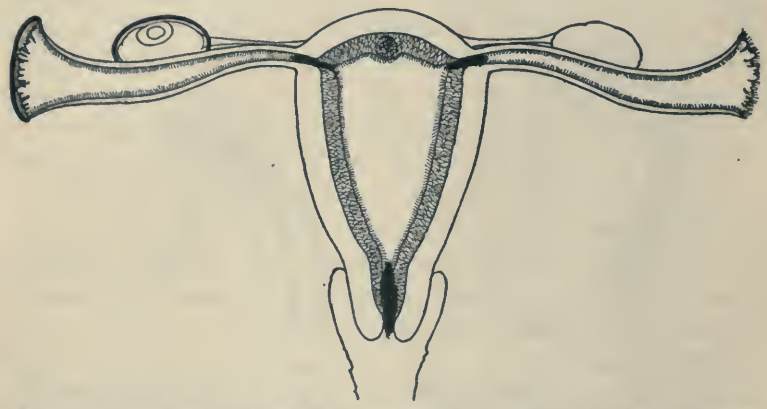

Fig. 176.—The dark lines show the location of inflammation—cervix, uterus, tubal cornua, adhesions about the tubal openings, about the ovaries.

with or without adhesions about the outer ends, with or without closure of the outer abdominal ends; you may have inflammation and adhesions about the ovary. If you have a yellow, greenish, thick, tenacious mucus pouring out of the cervix like a veritable Niagara Falls, you will find it impossible to readily remove it or to free it from the cervical canal. If you examine it with a microscope, you will get a pure smear of pus. To expect any spermatozoön to pass that obstacle, leaving aside the inflammation, is to ask too much. If you dilate a cervix of this kind, or any inflamed cervix, you are stirring up an active or a latent inflammation. If you curet a uterus whose lining is involved

by inflammation, you are doing the same or worse; for every gonorrheal cervicitis or endometritis lights up after a curetage. The bacteria thrive on the blood which is poured out, for human blood and human serum are the best culture-media for gonococci. If on bimanual examination you conclude there is no salpingitis —and such a diagnosis must be made cautiously—how can you exclude the existence of a salpingitis in the cornual area? One certainly cannot deny the possibility that it is present in that part of the tube. If by any chance, there is no evidence of an endocervicitis, and no marked signs of an endometritis, you cannot definitely deny the possibility of these conditions having improved without treatment in the course of time, and that they have left slight evidence behind. The milder forms of salpingitis may exist without any cervical signs.

Hence, if you curet any of these cases, you drive the inflammation from the uterus into the tube, or from the cornual area of the tube out through its whole length into the peritoneal area, adhesions form, and the very thing you should avoid has happened. You should never curet a uterus for sterility or dysmenorrhea; in fact, you should never curet at all until by repeated examinations you exclude an inflammation, and you should not do it any way when a patient's menstruation is normal or below normal. One thing must be impressed with the greatest emphasis, and that is, that you cannot cure an inflammation of the cervix or uterus by curetage. The lining of the uterus is not a membrane to be toyed with on the principle that it is readily restored. Even if no inflammation is present, a curetage may so affect the ovary that the patient suffers subsequently from varying degrees of amenorrhea. As between the endometrium and the ovary it is a case of "you tickle me and I tickle you." The ovary stimulates the endometrium; the endometrium grows thicker, the cells grow larger in anticipation of the next menstrual decidua, and the secretion thus produced in turn stimulates the ovary. If you remove too much endometrium, the ovary is injured and may atrophy. Except in cases of polyps or polypoid endometrium, in cases of fibrosis uteri where pregnancy is no longer a consideration—and here only after the exclusion of in-

flammation—I have not cureted to any degree for years; and even in miscarriage the curet is scarcely ever used. I hope that some day there will be a law that before we curet a patient we must get a license or permission from some central authority to use it in a particular case and then only after giving genuine reasons therefor.

Now, leaving the element of inflammation entirely out of the question, how about cervical stenosis, angulation at the internal os, etc., as the cause of sterility? The first questions always to be answered are: Are normal spermatozoa present? Is a ripe ovum thrown out? How do we know whether an ovum is thrown out at every menstruation, or even at irregular intervals? Between menstruations a ripening Graafian follicle grows so that it reaches the surface of the ovary, separated from the peritoneal cavity by only a thin membrane. This membrane (the outer covering of the ovary) is dissolved by an enzyme action of the liquor folliculi which erodes, allowing the fluid to be expelled, carrying with it the ovum. But suppose a follicle lacks that enzyme, and that it does not burst, does not liberate the ovum? It remains in the ovary and is an atresic follicle. If this process is repeated, one or both ovaries are filled with these little cysts, and it is often difficult or impossible for such ovaries to free any future ripening follicles as they attempt to approach the surface.

Why do certain ovaries lack this enzyme action of the follicle? Because something is wrong with the thyroid, adrenals, or pituitary which support the ovary in its activity. In addition, you have the inflammations whose invasion of the ovary leads to the type of small cystic degeneration. Hence we come to the conclusion that even a normal menstruation may not mean the throwing out of an ovum.

Now, if a woman menstruates only every two or three months, or at longer intervals, does that mean that she gives out no ova? No. I have seen many such patients become pregnant without any regularity in their menstruation at all. How about the woman who becomes pregnant while nursing a baby and who during this nursing does not menstruate? A nursing mother with amenorrhea is not supposed to be ovulating because the

action of the mammary secretion inhibits the function of the ovaries, and probably at the same time exerts an inhibitory action on the pituitary lobe; yet such women do ovulate, and we have thereby a proof that ovulation may take place without menstruation; so that varying degrees of amenorrhea, or even the more decided degrees of amenorrhea, are not necessarily a bar to fecundation.

Now, suppose that we are certain that an egg is thrown out from an ovary every month; and suppose we are sure from examination that normal spermatozoa are present; what gives us the right to locate the obstacle to fecundation in the cervix? May

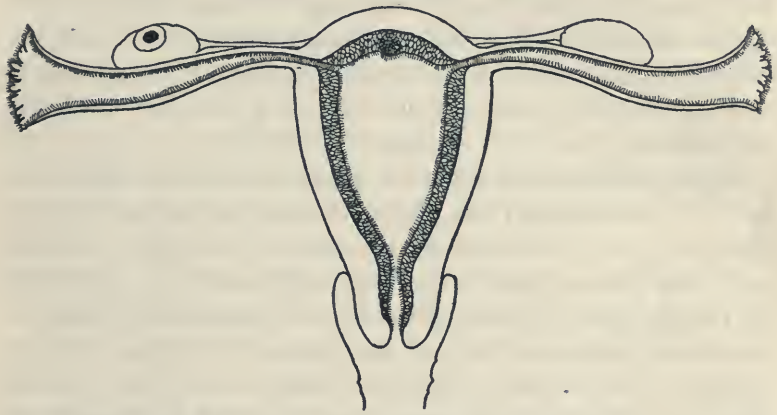

Fig. 177.—The ovum given out of its follicle moves through the tube, carried along by the cilia, and finally nesting in the lining of the uterus.

it not be the tube which is at fault because the cilia do not act? May it not be a failure of embedding and nesting of the ovum? Let us for a moment consider the earliest steps of pregnancy. Spermatozoa are deposited in the posterior fornix (Fig. 177). They pass up through the cervix by virtue of their own activity against the current of the ciliated epithelium in the endometrium. As you know, the ciliated epithelium in the endometrium waves downward toward the cervix. It is the nature of an energetic individual to surmount obstacles and not to always follow the current of ease. Men who make the biggest successes are those who do it in spite of opposition, and we may take these tiny

spermatozoa as an illustration. Why do they pass upward through the cervix into the uterus? It is because the current is against them; and they meet the same opposition in the tubes, for there the cilia wave from the abdominal end toward the uterus. If you cut the uterus at the interstitial area and see the caliber of the tube at this point you will see how extremely narrow is the lumen. If spermatozoa pass out through this canal and if fecundated ova are moved through it by the cilia into the uterus, why cannot a cervix that readily admits a sound offer a ready path for the upward moving spermatozoa? If a cervix is filled with adenoid overgrowths of the mucosa, if the internal os is lined by a lymphoid ring of this overgrown tissue, it is possible that the obstacle to the spermatozoa may be absolute; but in the non-inflammatory cases I believe we have tremendously exaggerated the rôle of cervical obstruction, and I have laid relatively little stress on the cervix as a cause for sterility.

Now, what happens when an ovum leaves the Graafian follicle? It is discharged into the peritoneal plasma and is drawn into one tube or the other by the current created by the cilia of the outer end of the tube waving toward the uterus. Through the tube it is pushed along on the tops of these cilia; and now we can readily understand why, if you have a tube on one side of the uterus with the ovary removed and a normal ovary on the other side with the tube removed, an ovum can be drawn from one side of the uterus over into the outer end of the tube on the other side. Inside of the tube is a microscopic ovum; inside of the tube are microscopic spermatozoa. It is interesting simply to wonder what attracts the spermatozoön to the ovum, so that the head of the spermatozoön may enter the ovum and fecundate it. When the egg is fecundated it enters the uterus, the outer cells of this growing ovum forming a cell layer called the trophoblast, which digests the surface of the decidua at the point where it is to settle. It burrows itself in this overgrown thickened mucosa, is surrounded by lymphoid exudate, and covered by a tiny scar. When this occurs, the trophoblast cells throw off a secretion which is absorbed into the circulation, and this secretion continues to be thrown into the mother's blood during the

whole nine months of pregnancy. The chorionic villi develop especially at the point where the ovum rests, and here ripens the future placenta. Hence if an ovum settles at the lower segment of the uterus we have the varying forms of placenta prævia. The secretion given off by the outer covering of the ovum nullifies the action of the ovary, thyroid, and especially the pituitary, which normally lead to menstruation. If this fecundated ovum cannot nullify this menstrual tendency, blood is poured out from the capillaries and the ovum is thrown out. In other words, many a fecundated ovum, by its inability to resist the menstrual stimulus, fails to remain in the uterus more than a few days. We have many patients who occasionally or repeatedly are a week or ten days over the period, and then menstruate, who undoubtedly represent this process. I have often told such patients not to worry, that some day by the aid of the internal secretions administered therapeutically we would so help the trophic processes concerned in embedding and nesting that normal pregnancy would take place; and, sure enough, it often does.

What can you do to help the egg to nest? We try to nullify the pituitary element. In these cases we don't wish it to have too much to do with the onset of menstruation. We give thyroid extract among other drugs, and you will find it a great help in many cases. If this idea of trophic support of the ovum in its attempt at nesting be true, the same idea will hold good during the whole two hundred and eighty days of pregnancy. The pregnant woman is trying to menstruate every twenty-eight days; and the ovum and its secretion is trying to stop it. If you can nullify the tendency to menstruation during the early weeks, why not attempt the same therapy during the other months?

Now the results of endocrine therapy in patients who have had repeated miscarriages are so excellent that it forms—next to the results obtained in amenorrhea—almost the most specific action we can use to serve as an illustration. Is it certain that the action of the endocrines holds only by aiding embedding? It is quite probable that in many of these cases of sterility we must assume that the ciliated epithelium as the result of insufficient trophic support is not functionating normally. If the cilia are not

active, they will not carry an ovum into the tube. Why not also take it for granted that some of the follicles of an ovary would break if you gave them sufficient trophic support. If we conclude that sterility is due to affections of the ovary, thyroid, and pituitary gland, and that ovary supported by thyroid and pituitary is concerned in the care of the genital tract and that they act together in the production of menstruation, then we must stimulate the genital tract by extracts of these glands. Whether they aid the bursting of follicles which would otherwise be atresic, or whether they stimulate the ciliated epithelium of the tubes to normal activity, or whether they aid the processes of embedding in a trophic way, is of no great moment in any successful case. So long as in many favorable cases, where two or three of these gland extracts are given, a favorable result is obtained, what difference does it make to us which function was aided by the therapy—whether the ovary, the cilia of the tubes, or the element of embedding?

Chart No. II discloses some of the knowledge we have concerning the ovary and other secretory glands, based on animal experiments made many years ago. I was fortunate enough to be acquainted with Knauer at the time he made those first studies on animals, with particular reference to the ovary. Ovaries were taken out of the young, with the result that the genitalia failed to develop. Ovaries were taken from mature animals, and the genitalia underwent atrophy. On the other hand, ovaries removed from their normal connections were transplanted into the mesenteric region or between the fascia of the abdominal wall, and whenever these were properly nourished and produced follicles the genitalia developed if the experiments were made in the newborn; and the genitalia were trophically sustained if these operations were made in mature animals. This proved that the ovaries exert their action by virtue of the secretion sent into the human economy.

You know the old idea concerning menstruation was that the ripening Graafian follicle distended the ovary, and the impulses from the ovary were transmitted to the spinal cord and thence to the uterus, causing the premenstrual and menstrual phenomena.

This would make menstruation dependent on the rhythmic and regular liberation of an ovum at or about the same time, and I think we have shown in our discussion already that ovulation, while it usually precedes menstruation, does not always do so, and that menstruation is dependent upon ovarian secretion liberated continually and continuously.

It is the result of these experiments and the results obtained by cauterizing the corpora lutea in the early months of pregnancy in animals (with the resulting expulsion of the uterine contents) that attracted attention to the corpus luteum as an important trophic element in connection with the genitalia and pregnancy.

We now come to the climacterium and its usually associated diminishing or disappearing menstruation, with a certain proportion of cases characterized by excessive menstruation. Normal menstruation represents harmonious team work on the part of the ovary, thyroid, and pituitary. As we have stated before, children with thymus affections, certain types of thyroid disease, definitely recognized pituitary anomalies, fail to develop their bones, or bodies, or their minds. Affections of this sort are not always of the major type with well-marked characteristics. There are varied and minor forms where only one or other of these phases is apparent; development is not parallel as regards all the functions; the affection may not have been sufficient to interfere markedly with the general appearance or health of the individual, and yet the genital development may be relatively negligible and may represent any of the varying degrees of hypoplasia. Then we have the woman or girl who has developed normally, who has menstruated regularly, and then, on the development of a thyroid, pituitary, or other glandular anomaly, has suffered a deterioration in the region of the sexual organs. Then we have the case of pineal, adrenal, and pituitary gland tumors characterized during life by marked precocious sex development; and tumors of the above-mentioned glands have been found at autopsy to have so altered the secretory activity of these important structures as to leave us in no doubt that these glands were responsible for the excessive development in the

sexual sphere. That leads me to believe that if children were fed with certain gland extracts at certain periods, with a definite purpose in mind, we could make of them physically, mentally, and otherwise far healthier, stronger individuals than when left to the mercy of their own internal secretory apparatus—which with every passing year we recognize to be in many instances inadequate to the needs of the body. The diseases of childhood,

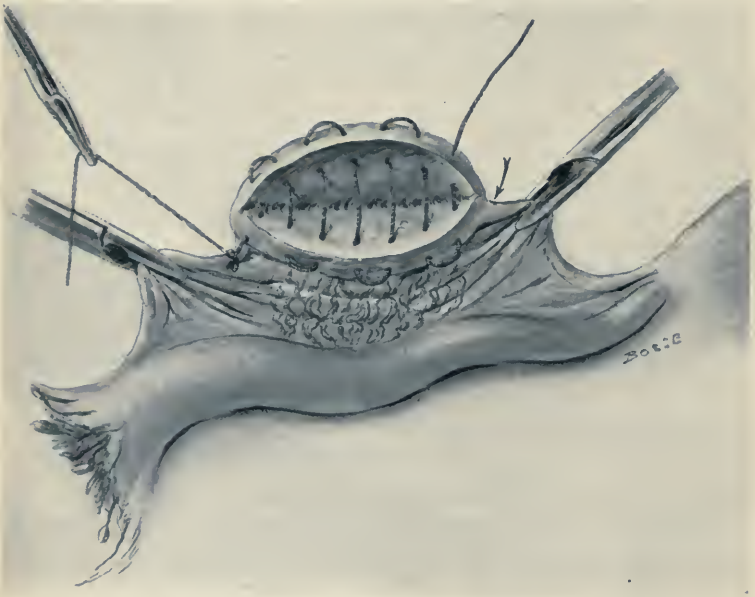

Fig. 178.—A wedge-shaped area is taken out of the convex surface of the ovary, removing all the cysts and corpus luteum rests. The raw surfaces are brought together by continuous suture.

such as whooping-cough, measles, scarlatina, diphtheria, mumps, etc., have in many instances an injurious effect on one or more glands of the body, and from our standpoint injury to the ovary and the uterus, and those glands which are associated with the trophic control over the genitalia, deserve the greatest consideration. Many cases of uterine and ovarian hypoplasia are to be referred to the injurious action of the diseases of childhood. If the toxic effect of these infections is centered on those elements

of the glands which preside over the mental and psychic states, we have an explanation of many of the mental and nervous affections of children for which no apparent cause has heretofore been brought under consideration.

We refer again to the harmful effects of the present influenza epidemic on the uterine mucosa, with its influence on menstruation. It is natural if that same injury takes place when the growing ovum is in the uterus that a tendency to miscarriage or premature labor should occur. I have had several cases of

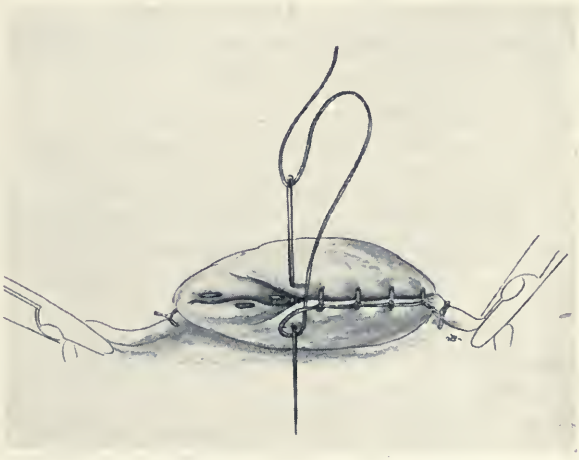

Fig. 179.—An interlocking suture covers the raw edges after the preliminary suture shown in Fig. 178.

pregnant women who after slight attacks of influenza began to spot and stain. They were put to bed, given a dose or two of morphin, and immediately put on ovary and thyroid extracts, with excellent results.

Figures 178 and 179 illustrate my operation for exsection of the cystic area in the so-called cystic ovary. Let me mention a patient who was sterile; married six years. Normal spermatozoa were present in the seminal fluid of the husband. Inflammation, judged by the severest tests, bimanual and microscopic, was excluded; no tubal inflammation was found. The patient was

put on endocrines, with no effect upon the sterility. My conclusion was: The endocrines, by their effect on the tubes and endometrium, have excluded inactivity of the cilia and failure of proper embedding as the causes of sterility; therefore ovulation does not take place in this patient. I opened the abdomen and found both ovaries cystic. Unless you find an actual corpus luteum from a recent ovulation present, you cannot tell from observation of the ovaries whether ovulation takes place or not. I removed a wedge-shaped piece from each of these ovaries, leaving behind only normal tissue free of cysts. The patient became pregnant within a few months. Therefore, just as I take out the appendix in every laparotomy, I excise this wedge-shaped piece from the cortex in every cystic ovary where laparotomy is performed, no matter for what purpose.

Figure 178 illustrates the method of sewing the ovary after excision. The No. 1 catgut suture begins at one end with a knot, and then passes through and through the ovary, uniting the raw surfaces together by a Connell suture until the other end of the excised area is reached. Then a knot is tied on the free edge of the mesovarium. The continuous suture then goes back over the raw edges (interlocking in character) until the first knot is reached, when the two ends are tied (Fig. 179). It is essential to be sure that hemostasis is complete, and an occasional interrupted suture is needed to obtain this result. I believe that the time is coming when this operation will be done very frequently, with sterility as the primary reason for same.

If we could assure our sterile patients with certainty that this operation would be successful we would find a ready response; but, however certain you may be, by excluding other causes and by the failure of endocrine therapy, that this ovarian condition must be the point at fault, it is too great a responsibility to guarantee success after this operative procedure. Several of my patients, however, have become pregnant after this operation; and even if to the carping critic I have not proved that the operation was the cause of the pregnancy, it certainly does prove that the patients may become pregnant after resecting a wedge from each ovary, and even after removing one ovary and resecting

a wedge from the other. In one patient I removed a dermoid cyst of one side and half of the ovary from the other, and she has since been delivered of two babies.

We must remember that when these cystic ovaries contain corpus luteum cysts, or corpus luteum nests, ovulation may be inhibited; that is the purpose of the true corpus luteum which develops after pregnancy takes place. This true corpus luteum body, supposed to aid and further the connection of the ovum with the uterine lining, is supposed to inhibit ovulation during pregnancy. So if corpus luteum bodies are retained in one or both ovaries, even though menstruation continues, I believe in many cases ovulation does not. Therefore, in removing from these ovaries not only the atresic follicle cysts but also the corpus luteum cysts, or corpora lutea, I believe we are allowing the processes of ovulation to be again restored.

The following chart shows some of the facts proving the relation of gland states and the infectious diseases of childhood and adult life to the development and conservation of the genitalia:

CHART No. II

1. Removal of ovary { Failure of genital development. / Genital atrophy.
2. Transplantation of ovaries { Genital development. / Preservation of genitalia. / (Internal secretion.)
3. Operative removal of ovaries: Menstruation not restored by endocrines.
4. Climacterium { Diminished menstruation—menopause. / Increased menstruation = ovarian and pituitary overactivity.
5. Physiology of menstruation { Ovary supported by thyroid and pituitary. / (Crisis).
6. Action of infectious diseases of childhood: Retard development.
7. Action of thymus, thyroid, and pituitary diseases on the development of the genitalia. { (*a*) Direct, (*b*) through the ovaries.
8. Action of thyroid and pituitary diseases on the preservation of the genitalia.
9. Pineal, adrenal, and pituitary precocious sex development.
10. Action of influenza on menstruation and pregnancy.

What are the facts of practical experience which tend to prove the value of endocrine therapy? It is over eighteen years

ago since I began to use ovarian extract and thyroid extract. Since then various other gland secretions have been put into our hands, and the experience gained by the successive use of the various extracts singly and combined has really meant the entire remaking of the therapy in gynecology. It is certainly one of the greatest pleasures in a medical man's life to have a woman menstruate regularly when her complaint has been a menstruation every five or six weeks, and then only for a day or so. Other women menstruate every three months; some, once a year. While some of these cases are not curable, if the process of atrophy has gone on too far or if the hypoplasia is too marked, yet in a large majority of instances the administration of ovarian plus thyroid plus posterior pituitary extracts, etc., with patience brings about the desired result.

Following is a little chart showing some of the facts which favor endocrine therapy:

FACTS FAVORING ENDOCRINE THERAPY

OVARY, THYROID, PITUITARY ANT., PITUITARY POST., THYMUS, MAMMARY, SUPRARENAL, ETC.

1. Action in varying degrees of relative amenorrhea.
2. Action in varying degrees of actual amenorrhea (no signs of endocrine abnormality).
3. Action in varying degrees of actual amenorrhea: Signs of endocrine abnormality—pituitary, thymus, etc.
4. Action in varying degrees of menorrhagia.
5. Action in threatened miscarriage.
6. Action after repeated abortions { Aids attachment. / Trophic.
7. Action in lactation atrophy.
8. Action in aiding fecundation—after one baby, with varying periods of delay.
9. Action during menopause of climacterium.
10. Action in sterility.

In speaking of sterility, we should make clear to ourselves what time must elapse in the marriage state before the patient can be put in the category of sterility.

I formerly took it for granted that if a patient was married a year and a half and was not pregnant, serious medical consid-

eration should be given to her condition; but today I have concluded that if a woman does not conceive within six months after marriage when no precautions are taken, or within six months after precautions are no longer taken, that sterility really exists. So, in taking the history, never fail to inquire not only how long the patient has been married, but for how long a period precautions were taken.

In order to arrive at the proper conclusions I took the cards of 80 of my own primigravidæ, and found that an astonishingly large number had been married from ten months up to four years, and several five and ten years, before fecundation took place. I then inquired directly or by letter as to how long a period precautions were taken; and subtracting this period I found that practically 95 per cent. became pregnant within three to six months; the very largest number, between one and three months.

One patient was married ten years and occasionally accompanied a pregnant patient of mine to the office. She had taken precautions. A former friend of hers had had such a difficult labor that she was too frightened to allow herself to conceive. When she saw her friend, this patient of mine, delivered with relatively little pain, she concluded that labor was not such a terrible condition; precautions were avoided, and she conceived at once.

Two patients who had taken no precautions conceived—one after eleven years of married life, the other after ten years. The former had visited many physicians; had been advised to have a dilatation and curetage done; had been told she had a floating kidney and a retroverted uterus; in fact, she had never consulted a physician without operation in one form or another being urged. Fortunately for her, she never followed any of the suggestions that were made, and as her health was poor she was given a rest cure, in the course of which she gained 30 pounds, and a few months later she conceived. The explanation is to be found in one of two possibilities: Either she had a form of salpingitis affecting the interstitial area of the tube which in the course of time healed; or some interglandular upset was righted in the course of time, and some trophic change occurred in the

uterus or the tubes, or in the ovary, that permitted ovulation, the carrying of the ovum into the uterus, and embedding, to take place.

The other patient was operated upon eight years ago—after being married two years—for double-sided pyosalpinx. One tube and ovary were removed; the tube of the other side was cleansed, and with the corresponding ovary was left in place. At the time I am now speaking she is three months pregnant. In other words, it took nature eight years to heal up the remaining tube sufficiently to restore its patency and restore the activity of the cilia.

In another portion of the chart you will see 5 patients, 4 of whom had half of each cystic ovary resected; while the fifth had a dermoid of the ovary and the tube of one side removed, and half of the cystic ovary of the other side. All have conceived. The operations were done for sterility.

In the table shown on page 951 are 50 consecutive cases of sterility. No matter what other complaints the patients had, I have taken no records except of those who when asked by me as the history was nearly completed: What are the two things of which you are complaining? gave as the first answer: "Why do I not become pregnant?" In other words, these patients came for an answer to this question.

In the first column you will see the patients in whom I found inflammatory conditions sufficiently marked to lay the blame on this state, with little reference indeed as to the question of spermatozoa. The diagnosis is written after each name. The names surrounded by a circle have been laparotomized by me, and the diagnosis in every instance verified—inflammation, with closure of the tubes.

Underneath you will notice two patients—one married ten years and the other nine months—whose conditions warranted operation. The first had a double tubo-ovarian cyst filling out the entire pelvis; the other, married nine months, whose menstruation lasted only one day, had a large fibroma of one ovary and a small one of the other.

The next column shows the cases in which the male element

INFLAMMATION			SPERMATOZOA			R SPERM. O. K.					
(2½)	(R)	Sooph d & sin.	12	A I	Refused Ex.	7 G c	Rep'd Ab. - Cer. Rel. Amen.	R	Sooph. - d - Exs.		
1½	ER	Diag. - Sooph d & s (no sp)	4	AC	Not potent	2 Gl	Menstr. q. 7 Mo.	KR	Dermoid - S - Exc ½D		
1½	(EA)	(Apdx) - Sooph d & s - Sp. poor	3	B	None	2 K	Menstr. q. 6 wks. 1 day. Stem	DR	Exc. bilat.		
3½	G	Cornual Infl. (Sp. O. K.)	14	S	None	8 W	Dystad. - Gen.	CR	Exc. bilat. Susp. Sten.		
4	M	Sooph d & s (Sp. O. K.)	10	R	Some active	4 R	Menstr. q. 4 - 7 Mo.	M	Exc. bilat. Susp. Sten.		
3 Yrs.	H	Curet, Abscess (Sp. O. K.)	6	SA II	None	2 SCH.	—	H	8 Mos	Thym. 2 Wks.	
+ +	(BL)	Sooph d & s.	6½	G	Sperm. Dead.	5 Ll	Pain right side	AL	9 "		
S	(K)	Sooph d & s.	8	GR	None "Mumps"	5 (LE)	Pain right side, "Mumps" Rel. Amen.	DR	9 "	At once	
7	BR	Tub. - Ov. Cyst.	15	(GO)	Dysm. (Not potent)			L	12 "	(Dyst.)	
8	(BRUL)	Tub. - Ov. Cyst.	2½	H	None	M		BT	12 "	2 Wks.	
13 Yrs.	(M)	Curet, Absc.	6½	F	No sperm.			R	12 "		
			8	RO	None			K	17 "	Sp.	
TUMORS OV.			8	R	Cervix, Inactive, Sper.	2 K		M	18 "		
10	(ET)	Ov. cysts.	6	J	Cervix op.			SHR	24 "	R to Mr. Sp.	
¾ Yrs.	(D)	Fibroma ov.						BM	24 "	Pain	
								SHD	27 "	Dyst.	
								ROS	6 Yrs.	Menor. Curet	
										Menstr. q 40. - 78 days	

℞

The table shows four columns, the first being a list of cases in which inflammation of the tubes and ovaries were the cause of the sterility; the diagnosis was verified by operation in the cases which have a circle about the name. The two cases at the bottom of the first column were cases of tumor of the ovary; both were operated on. The second column shows cases in which the spermatozoa were at fault. The third column shows the cases where menstruation was markedly diminished and where, in spite of endocrine therapy, no favorable result was obtained.

The last column shows successful cases, the first five becoming pregnant after a resection operation on the ovaries; the others becoming pregnant after endocrine therapy only. The figures before and after the initials in each column show how long each patient was married; the figures before the initials meaning years; after the initials, meaning months.

was either lacking or so deficient that the responsibility for the sterility does not rest on the female.

In this column you will see a vertical line after some of the names, which means that they were either cureted or some cervical operation was done on them. It is needless to say anything further. One of these patients was cureted twice. No criticism is too severe to be vented on a physician who curets or dilates, or does a cervical plastic for sterility without first finding out whether or not spermatozoa are present.

The next column shows those patients in whom endocrine therapy has so far failed to result in pregnancy. It is needless to say that examination has proved spermatozoa to be present and active. With the exception of 2 patients, one of whom was cureted several years ago, none menstruates normally either in amount or with any degree of regularity. One menstruates every seven months; another, every six weeks for one day; another, every four to seven months, etc. Three of these patients are of the type of dystrophia adiposogenitalis. Under endocrine therapy menstruation has improved in practically every one, but as yet only one has conceived since this table was made out.

Now, as to the question of operation on these patients—whether they have cystic ovaries or not, or whether they ovulate or not—I have come to the conclusion, as a result of operation on several of this type of patient, that resection of part of each cystic ovary promises a favorable result only in those patients whose menstruation is regular, normal in amount, or excessive.

The next column shows the patients who have become pregnant: 5 after operation on the ovaries, and 12 as the result of endocrine treatment.

Patient H. was married eight months; had taken no precautions, and was in tears because she had not conceived. Her menstruation was excessive, lasting six days, with clots. The uterus was not large, but because of the excessive menstruation I gave her thymus extract, which she began to take two weeks before the next expected menstruation; which, however, she passed, and nine months later was delivered of a baby.

The next patient was married nine months. Her menstruation was only slight, lasting a day or two. She was given ovarian and thyroid extract, became pregnant, and was delivered of a healthy baby.

The next patient was married nine months. Menstruation was normal. She was put on ovarian and thyroid extract two weeks before the next expected menstruation. Her husband was requested to send me a condom specimen. She passed her next menstrual period, and is now under my care awaiting delivery.

Mrs. S. H. D. was an interesting case. Here was a patient who menstruated every three months. As the result of endocrine therapy she menstruated normally for two periods, and then came to me after a lapse of three months saying that the medicine had failed to produce a regular menstruation and that she had relapsed into her old state of amenorrhea. Examination showed that she had a genuine cause for this last amenorrhea of three months, the cause being a growing ovum in the uterus. She completed her labor in a perfectly normal fashion, even though the duration of her pains was longer than usual.

It is with me quite a usual experience to note that those patients who become pregnant only after gland stimulation do need pituitrin and that the labor lasts longer than is usual. One would expect this as a matter of course, for all these patients are to be viewed as having a certain interglandular dysfunction. The most interesting was Mrs. R. O. S., who became pregnant after being married six years. When she first came to me she suffered from intractable menorrhagia which yielded only to a thorough curetage. For years afterward she menstruated at intervals of forty to eighty days, which yielded and improved under endocrine treatment. Because this patient finally became pregnant after having given up hope, and because we were dealing with a well-developed baby, and because on the basis of previous experience I feared the labor would be either very long and demand much pituitrin or would eventually need the application of forceps, I delivered her by cesarean section. The interesting point is that she suggested this operation of her own

accord, because she felt from what she had read of the subject that it was the safest, surest, and quickest means of insuring her a live baby.

Of the cases which did not respond to treatment (col. 3), one menstruates every seven months, and was not at all faithful in taking the endocrines. Another menstruates every six months for one day; with the endocrines, her menstruation lasts two and a half days. Another patient, a pituitary dystrophy, menstruated every three or four months; but with endocrine menstruates regularly. Another is the most typical of pituitary dystrophies, who with the aid of endocrines given by mouth and hypodermically menstruates regularly for two and a half to three days. Another patient who formerly menstruated every four to seven months has continued the endocrines for a long period and her menstruation is almost normal.

So in these patients we are dealing with profound pluriglandular upsets, all characterized by diminished menstruation. It is for this reason that we do not consider them proper patients for abdominal operation on the ovaries; and my experience in this matter has shown me that we may expect a favorable operative result only in such patients as menstruate fairly regularly and in a fairly normal amount without endocrine stimulation.

Just a few words about the treatment of the male. If by substituting those endocrines which normally exist and normally exert a trophic and stimulating action on the ovaries, tubes, and endometrium we can thus aid the processes leading to fecundation and embedding, the same trophic and stimulating influences may be exerted on the structures which produce the spermatozoa; therefore, the same gland extracts should be used, with the substitution of testicular extract for ovarian extract, when the spermatozoa are not sufficiently active. In several cases I have treated the husband on this theory after examination of the spermatic fluid showed the spermatozoa to be not normal, and in the future I will give added attention to this phase of the question.

Of the gland extracts which are used, ovarian extract is given in doses of 7 to 10 grains of the whole gland. Ovarian

residue has been given in several cases by hypodermic—this being an extract of the ovary minus the follicular tissue. I believe this to be a very important part of the ovary.

Thyroid extract is given, as a rule, in doses of $\frac{1}{10}$ to $\frac{1}{6}$ grain three times a day. Larger doses than this I rarely give.

Suprarenal extract of the whole gland is given in doses of 2 grains. From a study of the histology of the adrenals, from our knowledge of its secretion, and from changes which occur in the cortex during pregnancy the cortex is the more important element from the standpoint of the gynecologist.

As to the pituitary extract, it is the posterior lobe which furnishes us with the element having a trophic and stimulating effect on the genitalia. The dose of this is $\frac{1}{2}$ to 2 grains three times a day. Its effect in stimulating is pronounced. It is the important part of the pituitary gland in the various types of amenorrhea. The anterior lobe, as already stated, has a marked influence on growth, and during pregnancy we frequently see evidences of its well-known hypertrophy during this period in the growth in stature, in the acromegalic change of features, and in the tonic effect which it has. From my observations, it has an effect on the feamle genitalia opposite to that obtained by the posterior pituitary lobe when administered, especially if mammary extract be added; it has a decided effect in reducing the size of the uterus. Therefore I do not use it in any form of amenorrhea. If given for its tonic effect in any case, this fact should be borne in mind, and posterior pituitary or ovary, or thyroid should be added.

Mammary extract is given in doses of 7 to 10 grains or more, three times a day, for menorrhagia, metrorrhagia, for fibrosis uteri, for myomata, or fibromata. As just stated, it acts particularly well when combined with anterior pituitary extract.

Thymus extract is given in doses of 5 to 10 grains three times a day. It is of value in the various forms of menorrhagia and metrorrhagia due to overactivity of the ovaries, and possibly acts well when the posterior pituitary is overfunctioning.

Placental extract, which is not yet on the market, but with which I have been experimenting for over a year and a half,

acts well in certain forms of dysmenorrhea and in certain forms of menorrhagia and metrorrhagia.

With these preliminary statements in mind, one may understand the following drawing (Fig. 180).

In the center are the ovaries and the genitalia. Beneath are the gland extracts, which lift up, support, or stimulate the ovaries and the genitalia. They are ovarian extract, thyroid extract, suprarenal extract, and extract of the posterior pituitary lobe.

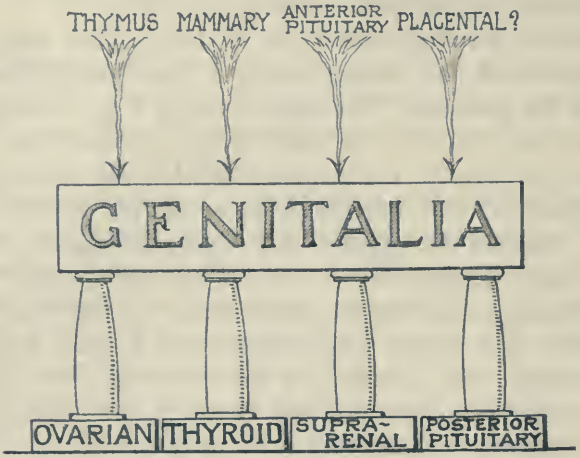

Fig. 180.

Above the ovaries and the genitalia are the gland extracts, which depress or inhibit the action of the ovaries and genitalia. These are thymus extract, mammary extract, anterior pituitary lobe extract, and probably placental extract.

With this figure in mind, one can see the basis on which to build up a system for administering these substances when the functions of the ovary, tube, and uterus are under consideration. But this is not all that we gynecologists have to bear in mind in treating our patients. We have to take into consideration the symptoms of diverse types from which they suffer—their gastric disturbances, their premenstrual phenomena, their headaches, their nausea, their nervousness, their states of mental

depression and excitation, as well as their minor and major forms of psychosis. Every one knows the symptoms belonging to a typical case of Basedow's disease, and such cases may be recognized at a glance; but there are thousands of patients who have hyperthyroidism without exophthalmos or without goiter, or without persistent tachycardia, which nevertheless can be recognized as hyperthyroidism. There are still others who at one time or another under the stress of physical or mental irritations give evidences of annoyances which can be attributed only to temporary or transient attacks of hyperthyroidism. It is the recognition of these masked types which may or may not be associated with true gynecologic abnormalities that must engage the attention of all earnest medical men.

Undoubtedly, the greatest difficulty in the proper interpretation of interglandular upset depends upon the fact that so many of the cases are of minor degree—of a degree less than is typical of the well-exemplified cases.

If we have exophthalmic goiter on the one hand and myxedema on the other; gigantism or acromegaly on the one side, certain types of dwarfs or dystrophia adiposogenitalis on the other; if we have fibrosis uteri and fibromyomata on the one hand and dystrophia adiposo genitalis on the other; if we have tetanus and paralysis agitains on the one hand and myasthenia gravis on the other; if we have excessive sexual and physical development due to tumors of the pineal, the hypophysis, and the adrenals and testis on the one hand and cases of undeveloped genitalia and infantile uterus on the other; if we have acromegaly on the one hand and osteomalacia on the other; if we have excessive function and menstruation through oyster ovaries on the one hand and diminished function and relative amenorrhea through ovarian hypoplasia and degeneration adiposogenitalis on the other; if we have the extreme adrenal disease known as Addison's disease, why may we not expect minor degrees of involvement in the glands or pluriglands responsible for these major cases, the resulting symptoms here often lacking the typical earmarks which define the standard types of which we have made mention?

If instability of gland function is transmitted, we have a new basis for predicating the various types of abnormality which may be inherited. Inherited instability of the thyroid may lead in the progeny to either myxedema or to exophthalmic goiter, or to variations between these two extremes. Inherited instability of the hypophysis may lead to small stature or to large growth, or to simply the psychic manifestations of dyspituitarism. *So that one member of a family may inherit from his parents or grandparents these somatic changes due to gland anomalies; or one may inherit the nervous tendencies or the instability of the nervous system, or psychoses resulting from anomalies of the internal gland secretions.*

We must distinguish between the somatic and the mental or psychic side of pathologic states due to the endocrine relation. I have seen in so many of my patients attacks of mental depression and blues, so many cases of excitement and states of exaltation of minor degree, so many cases where the states vary from slight exaltation to slight depression without apparent cause, cases after labor with depression of a mild melancholic type, that long ago I came to the conclusion that we must grant variations in intensity in mental diseases.

If we have the forms known as manic-depressive insanity, dementia præcox, melancholia, etc., why may we not have minor types of the same conditions confronting us in our gynecologic obstetric work? We know the excitability connected with the various grades of hyperthyroidism; we know the mental apathy associated with the various degrees of myxedema; we known the mental peculiarities and the changes in character in patients with hypophysis alterations. *All these variations, noted from time to time in my experience, have convinced me that mental diseases of extreme type may have the same relation to the milder forms and to the so-called neuroses and psychoses, and to the so-called neurasthenia and hysteria, that the major forms of exophthalmic goiter and myxedema, gigantism and dwarfism, etc., bear to minor variations noted every day.*

CONTRIBUTION BY DR. WALTER TIMME

NEUROLOGICAL INSTITUTE

A NEW PLURIGLANDULAR COMPENSATORY SYNDROME

INTRODUCTION

FROM observation and clinical examination of many patients throughout the past six years at the Neurological Institute of New York City I have come to the conclusion that the so-called types of endocrinopathies, such as status thymicolymphaticus, giantism, infantilism, acromegaly, and a host of unnamed others, are not static states, as one would be led to suppose from descriptions in the literature, but are simply cross-sections taken at intervals in a dynamic, progressive, and wide-spread disturbance of the internal glandular system. We had been struck at the Neurological Institute by the constant repetition of patients showing similar symptoms and similar physical signs which heretofore had been generally accredited to the asthenias accompanying neurasthenic states. The patients were usually of the late adolescent period, in the early twenties, and, to neglect for the present the detailed symptoms which we will go into later on, the outstanding complaints, overshadowing all others, were headache and muscular fatigability. Accompanying these two suggestive conditions there was an additional statement that they had been growing very rapidly for the past few years. We went deeply into their antecedent history and their family history and were enabled thereby to find many points of resemblance in these various individuals. One case, observed for six years, went through various stages to recovery at the age of thirty-two years. From his early history we recognized symptoms that are presented by cases in the beginning stages of this syndrome, notably the headaches, fatigability, and the skeletal growth. Cross-sec-

tions at various stages of his further progress also resembled clinical pictures in patients that had formerly been somewhat puzzling to analyze.

During the past three years so many cases of the kind have been observed that from our past experience we have been enabled to foretell, to a degree, the progress such cases would make. To add to this assurance, lately it has been my privilege to see many patients admitted to the hospital for divers complaints of middle age, in whom we recognized the final compensatory stages of this syndrome. Upon close questioning, their antecedent history bore out the facts that our studied clinical types presented to us in various stages of the syndrome. They were completely compensated cases and their presence in the hospital was for some entirely adventitious cause. Our observation has disclosed: clinical types presented by single cases at various ages and stages of the syndrome; progressive cases, observed over periods of from one to six years, which show the changing and probably compensatory nature of the disturbance; completed cases in which the disturbance had come to a definite stop, in which the antecedent history revealed the close relationship to our isolated cases which were still in active progress; uncompleted cases in which the condition, after passing through the preliminary stages, remained indefinitely progressive. It has been impossible, as yet, to observe one case from the beginning to the end of the syndrome—a period which varies from ten to twenty years—and until this can be done we must fill in the gaps as best we may.

GENERAL DESCRIPTION

This new syndrome, pieced together as described above, may be generally stated to begin in youth some years before puberty, and go through its varying stages in about twenty years. In its incipiency (*first stage*) it presents largely the characteristics of the so-called status thymicolymphaticus, or status hypoplasticus of Bartels. There is complaint of muscular fatigability as a subjective sign with frequent accompaniment of headache. Objectively the case presents usually, though not invariably (for

exception see Case III, Fig. 186), an insufficient genital development, with perhaps inversion of sex type, with a penis that emerges from scrotal folds of labial type, or cryptorchism, or both. In the female the menses are usually delayed, the uterus and ovaries remain infantile, and there is scarcity of pubic hair. Blood-pressure is usually low and blood-sugar content low. Enuresis is common. There is usually present the white line of adrenal insufficiency of Sergent.

In the *second stage*, that beginning at puberty, we find a continuance of the muscular fatigability or even an increase. The genitals may remain backward or invert in development, the pubic hair is sparse and has the distribution of the opposite sex, the male showing a horizontal demarcation, while the female has the pyramid type in which the middle line to the umbilicus shows a hairy tendency. Axillary hair is absent and chin and lip show no signs of hair in the boy. Blood-sugar is low, usually below 0.070 per cent., and blood-pressure below the normal. The white adrenal line may be elicited, especially marked after fatiguing exercise. Roentgenograms of the skull usually show a sella turcica which is small or which may apparently be even enclosed by the clinoid processes. This is an important point to determine, for the later progress of the disorder presumably depends upon the capacity of the pituitary gland to become hyperplastic. The size of the sella turcica, therefore, plays a determining rôle in the production of the later symptoms. The possible excessive function of the pituitary later on dominates the picture and is conducive to compensatory cure. The thymus gland frequently is seen in the *x*-ray picture as quite enlarged. In some cases of extreme fatigability I have also seen pineal shadows. During the second stage rapid growth in length begins to become manifest—not ordinary normal growth—but rapid in the extreme, so that 5 or 6 inches in height a year is frequent. With this growth fatigability increases, and it is on this account that the case is first brought to our attention.

In the *third stage* we begin to see the results of some of the compensatory activities. It is usually ushered in about the twentieth year of life. Growth has continued until the patient

is 6 feet high or over; his weakness, even though his musculature seems splendid, is his prominent symptom. He shaves rarely or never. Pubic and axillary hair remain as before. Now he begins to notice an enlargement of his hands and feet, and a frontal headache or, rather, an intratemporal headache comes on. Blood-pressure remains low (90 to 100 millimeters systolic), blood-sugar usually remains low, but now frequently rises as compensation progresses. Our patient shows decided vagotonic symptoms. An *x*-ray of the skull at this stage, or during this stage, if the case progresses favorably, shows a sella turcica which, while small, may show erosion of the clinoids and a deepening of the cavity. This tendency of the pituitary to become hyperactive produces the headache (if the sella is contracted), the increase in blood-sugar content, the growth of hands and feet, and a gradually rising blood-pressure.

The *fourth stage* now comes on from three to ten years later. This is the stage in which either complete compensation is produced or else the untreated case takes on the varying and various attributes produced by an enlarged pituitary body engrafted upon the earlier manifestations of a thymic state. That is, we have in the completely compensated case features of acromegaly, although the blood-pressure and blood-sugar are normal and the headaches have gone. The sella turcica on *x*-ray examination seems large. In the uncompensated cases we usually see a sella which is still small and perhaps bridged, with headaches of increasing severity, perhaps attacks of petit or grand mal, dependent upon the disturbance of pituitary function, mental torpor, increase of weight with constantly increasing fatigue, and a final lethal termination in itercurrent disease.

A brief résumé of the characteristic symptoms and findings in the different stages is here succinctly put forth:

First Stage.—The bony structure shows various endocrine anomalies and defects; disproportion of various skeletal units; teeth late and usually characteristically anomalous, so that the lateral incisors are very small, the central incisors disproportionately large, the canines of the type of incisors with a cutting edge instead of a tearing point; epiphyses slow in joining shafts

of bones; hyperextension of joints; hair growth late and sparse; cramps in muscles; tendency to hemophilia and spasmophilia; enlarged thymus; maxillary torus; tonsils large and adenoids present; low blood-pressure; low sugar content of blood; epistaxis; cyanosis of extremities; fatigability; small sella turcica; enuresis; low CO_2 coefficient of the blood.

Second stage begins at about age of puberty; rapid skeletal growth begins; late menses and small or infantile uterus; great fatigability with all evidences of low adrenal supply—low blood-sugar; low carbon dioxid combining power of the blood; white line of adrenal insufficiency; pubic hair of invert type; lack of hair on face and chin and axilla; smooth soft skin of child; genitals of invert type or else retarded; vagotonia; symptoms of hyperacidity and gastric ulcer; enuresis; undue length of long bones; low blood-pressure; little stamina.

Third Stage.—Twentieth to thirtieth year; beginning gigantism; headaches, pituitary in character; drowsiness; acromegalic beginnings or other pituitary stigmata; fatigability may continue or improve; mental confusion and hebetude; epileptiform attacks, uncinate in type; sella turcica enlarges or else erosion of sella or clinoids takes place; blood-sugar gradually increases if a cure is established. In uncompensated cases mental symptoms, moral and intellectual deficiencies and delinquencies arise.

Fourth Stage.—Either complete compensation, so that the patient may live comfortably within limits of exertion, or else may progress to the end of life as a pituitary case. The various external manifestations of pituitary disturbance remain even if the physiologic cure is complete. Blood-pressure rises; headaches cease; fatigability vanishes.

DISCUSSION OF SYMPTOMATOLOGY

The bony structure in the first and second stages usually shows anomalies in proportionate skeletal growth, *i. e.*, legs too long for thorax or vice versa (my scale for this determination is a fraction with the numerator as the distance from the sternoclavicular junction to the anterior superior spine of the ilium of the same side, and the denominator the distance from the anterior superior

spine to the external malleolus; normally, this fraction is one-half—a larger one meaning too large a torso, while less than one-half represents too long a leg; I call this ratio the torso-leg ratio); the joints are usually hyperextensible and frequently the ligaments are so relaxed that dislocations are easily produced. The extremities can be thrown about like flails; while the teeth are usually delayed in their appearance they also show certain characteristics. The lateral incisors, especially in girls, are frequently greatly underdeveloped. The canines, likewise, are either underdeveloped or else take on the flat appearance of incisors, losing their fang-like appearance. With the cyanosis of the extremities we occasionally get a pustular-like eruption about the nails. The symptoms during the second stage may need some elucidation. The so-called "white-line" of adrenal insufficiency was first described by Sergent. It has not been proved to be due to the deficiency, but in my experience it invariably accompanies low blood-pressures, and may be made to disappear very quickly after a hypodermic injection of adrenalin. Previous emotional disturbance, even so slight as that produced by standing before a camera to be photographed, will make its appearance impossible to obtain. It is obtained best by having the patient lying quietly in bed for a short while and then stroking the skin, preferably of the abdomen or thigh, lightly with the palmar surface of the index-finger. In ten to twenty seconds there will be a blanching of the skin thus stimulated. (See Sergent's article, Endocrinology, 1917, 1, 18, for the explanation of this phenomenon.) The low carbon-dioxid combining power of the blood plasma diminishes the so-called "buffer" property of the blood and leads to acidosis on slight provocation. The smooth soft skin of these cases, even in the third decade of life, with little or no secondary hair on the face, a faint suspicion of lanugo on the lip and chin, and a "peaches and cream" complexion, frequently stamps these cases at sight. The headaches, produced as will be discussed in the pathogenesis, are of a specific type. They are invariably stated to be between the temples, the patient indicating the locality by putting one index-finger on each temple, directed mesially. We have come to call them "pituitary headaches."

The vagotonia present in many of the cases frequently takes on the character of hyperacidity of the gastric juice with frequently symptoms of gastric ulcer, spastic constipation, and eosinophilia. In the third stage the symptoms of great interest are the mental ones. In many years' observation of pituitary disorders we have been frequently struck with the mental quips of the hypopituitaric. He exhibits lack of inhibition of the emotions, becomes highly excitable on little cause, alternating with sluggishness; frequently has phobias and compulsions (one case was a true kleptomaniac), shows frequently moral and sexual obliquities; and exhibition of pituitary feeding often modifies these characteristics. The symptoms of the uncompensated cases usually merge into those of a frankly dyspituitary syndrome. Blood-sugar disturbances, intense fatigability, periodic headaches, temperamental unfitness, and drowsiness are among the prominent symptoms.

ETIOLOGY

In practically all our cases there have been family histories of importance as regards endocrinopathies. Frequently parents or grandparents have shown such disturbances as diabetes, goiter, or acromegaly. A very common complaint is giantism. Collateral branches, too, show similar disturbances. Thus, W. W. (Fig. 190), the fully compensated case, has four cousins all afflicted with Graves' disease. There appeared in our cases no particular antecedent disabling disease or injury. One case, now in the second stage, had two brothers, both dying suddenly after exertion without known cause, in youth—possibly a so-called thymic death. Periodic headaches are also distinguishing marks etiologically. Menstrual disturbances of all kinds are met with here, especially the late-appearing type with lack of periodicity.

DISCUSSION OF PATHOGENESIS

During the first stage we see a clinical picture which is dominated by the characteristics of the status hypoplasticus of Bartels. The anomalies have been variously credited to hypofunction of the individual endocrine glands, excepting the thymus, which is supposedly hyperactive. Thus, Tandler and Gross

and Tandler have described many of the features of such a condition due to deficiency of the gonads. And yet, in direct contradiction to their view that gonadal deficiency produces growth in height with late joining of the epiphyses, I have seen cases in which at the age of eighteen with no menstrual flow yet established, the sexual apparatus quite infantile, the *x*-ray of the long bones showed the epiphyses almost united; the height of the patients being under 5 feet. Wiesel, Schur, and Schmorls and Ingiers have given both clinical descriptions and histologic and pathologic findings in such hypoplastic conditions referable to underactive or inhibited adrenal glands. Many observers have described the smallness of the sella turcica. My own observations agree with these. All of our cases show the smallness of the sella turcica in the early stages and, in addition, many of them have the bridging over by the clinoid processes, evident on *x*-ray examination. With these deficiencies of glandular structure and their diminished physiologic activity *ab initio*, the organism would of necessity come to early grief if some corrective were not forthcoming. Many cases do succumb early. Undue exertion, sudden excitement, narcosis, are all critical moments for such organizations, many of which cannot survive them. After puberty should have been reached (the second stage) the deficiency of the gonadal inhibition to growth (Tandler and Gross) is claimed to be responsible for the extreme height rapidly reached by our cases. One of our cases (Private B.), however, rather opposes this theory, in that the gonadal system early became hyperplastic and still the growth in body took place. This excessive genital development may be due in his case to an early involution of the pineal gland, for in the *x*-ray calcification of the pineal is seen. (Some authors hold that the overactive thymus with disturbed calcium metabolism is the cause of such "thymic giantism.") The deficient adrenal-chromaffin system is to be credited with the great fatigability, the low blood-sugar content, the low blood-pressure, and the white line. Now comes the third stage, the all-important one. It is in this period that the outcome of the syndrome is determined. In our judgment it is the pituitary gland which is here the critical factor. As we have seen, it

is invariably enclosed in a small sella turcica and possibly even hemmed in by the clinoids. Among its functions we have as all important a blood pressor principle and a sugar mobilization factor. Both of these are deficient in our patient. If the pituitary possibly could become hyperplastic and hyperactive with an intensification of these important properties, compensation might be accomplished. Such tendency to hyperplasia in a small cavity would of necessity through pressure produce headaches—an invariable symptom in the third stage of the compensated cases. And such headache would continue until the enlarged gland through erosion of its bony capsule or through pushing apart the clinoids made sufficient room for itself. As will be seen, these headaches continued for two to three years in some of our cases. Synchronously with these headaches, other incidental features of an enlarged pituitary gland became manifest: (*a*) acromegaly, lasting until the headaches ceased and the process then likewise ceasing; (*b*) a higher blood-sugar content; (*c*) a higher blood-pressure; (*d*) a diminished sugar tolerance. To make this view of the nature of the process of compensation more tenable many of the sellæ turcicæ of our patients in the second and third stages show erosion of the anterior or posterior clinoid processes; and in the final stage, an enlarged sella with practically no clinoid processes left at all. In the cases in which no compensation was effected—*i. e.*, in which fatigability and the other symptoms remained and progressed—the sella showed no enlargement (notably that of T. R., Fig. 192). In these cases we had headaches, periodical in type, adiposity, mental and moral deficiencies, petit mal, and other manifestations. Curiously enough in all our cases, the feeding of the pituitary gland in fairly large quantity disposed of many and at times of all these symptoms. But if the feeding were diminished or stopped, the symptoms reappeared. It seemed analogous to thyroid feeding in myxedema. One case, which gave a typical early history and seems uncompensated today at the age of forty-four, still shows the very small sella turcica with a clinical picture of abnormal bony structure much resembling Paget's disease. On pituitary feeding, this case is improving markedly in its fea-

tures of fatigability, headaches, and heaviness of extremities. It is too early to state whether in her case the cancellous condition of the bones will be restored. Finally, the fourth stage is ushered in by a gradual cessation of the fatigue, amelioration of the headaches, restoration of a normal blood-pressure, and normal sugar content of the blood. But the adventitious signs of the disturbance of the pituitary gland remain. Thus the fully compensated cases may show acromegaly more or less marked; *and this acromegaly is not to be taken as a diseased condition needing treatment, but simply as the hallmark of a process that has come to a stop—a self-curative process.* It is analogous to the hypertrophied heart become so through the deficiency of the cardiac valves and making up for such deficiency by its enlargement. And that condition likewise, *per se*, needs no treatment. A case that presents acromegalic features, therefore, need not necessarily be a case that calls for therapeutic intervention. It may well be a "finished" case. W. W. (Fig. 190) is a good representation of this type. These "finished" cases must always, however, live within certain limits of exertion and stress. The cases that in the fourth stage do not spontaneously go to full compensation are those in which we either find a sella turcica which did not enlarge (perhaps because there was no spontaneous effort of the pituitary to become hyperactive) or in which an enlargement of the sella did take place and the pituitary even in its hyperactive condition was not sufficient to compensate. These uncompensated cases go right on with progressive symptoms of fatigability, asthenia, headaches, and so forth, making them easy prey to intercurrent affections.

TREATMENT

The treatment of these cases in any stage is extremely satisfactory. The great point to remember is the probable nature of the process of compensation which the organism is endeavoring to carry out. That would make one believe that suprarenal gland therapy is indicated throughout on account of the patent deficiency of this organ in these cases. And yet in our hands its administration is disappointing. The whole gland perhaps has given better results than adrenalin, although the latter, either

hypodermically or (even against the dictum of the physiologist that it is inert when administered per os) by mouth in larger doses is good to tide over exceptionally bad days of fatigue and exhaustion. But the prime agent—almost a specific one—is pituitary gland in some one of its varied forms. Whole gland feeding in fairly large doses (2 to 3 grains t. i. d.) may be given in appropriate cases. But usually the dosage should be much smaller, and given at greater intervals; $\frac{1}{2}$ or $\frac{1}{4}$ grain every second or third day has given success in several patients. Occasionally, pituitrin hypodermically 0.50 to 1.00 c.c. per day or alternate days for one or at most two weeks at a time is excellent as supplementing the feeding of pituitary gland. Occasionally, in cases with pronounced genital delay, anterior lobe pituitary gland gives fair results. In those cases with vagotonic symptoms, hyperacidity, and conditions resembling gastric ulcer, atropin in doses to physiologic tolerance is indicated, and gives results. But the pituitary feeding in itself alone produces highly satisfactory improvement in almost every case. Under its use the headaches disappear, the fatigability diminishes, the blood-pressure and blood-sugar content increase, and the case goes on to cure. Gradually the pituitary feeding can be diminished and finally discontinued. In the older cases, in which the sella persists in remaining small (T. R., Fig. 192, and J. S., Fig. 191), constant feeding would seem to be necessary; at all events, the patients relapse as soon as treatment is stopped. Indeed, the patients themselves reach that point of accuracy of judgment in feeding the gland to themselves that they can determine the size and frequency of the dosage necessary to maintain them comfortably.

CASE HISTORIES

The following case histories are cited as a few among many which show characteristics of the different stages of the syndrome. Only facts having direct bearing are introduced into the case histories.

Case I.—J. M. (Fig. 181): Ten years; mentally backward; no hair on body anywhere; genitals undeveloped; elongated thorax; spasms in muscles; great fatigability; is a bed-wetter;

joints are hyperextensible; has nosebleeds. *x*-Ray of chest shows thymus (Fig. 182); skull shows small sella turcica, entirely bridged over (Fig. 183). Blood-pressure 85; white adrenal line.

Discussion.—This case is presented simply to show the type from which arise the cases presenting the later features of the syndrome, and hence may be classed under stage one.

Fig. 181.—J. M. Case I. Shows abnormal length of thorax compared with legs. Thighs especially short compared with lower leg. Small genitals. Has large thymus and enclosed sella turcica.

Case II.—Master F. J.: Age thirteen and one-half years; height, 61½ inches. He was brought to the Neurological Institute on account of his predilection for lying and, further, for his rapid fatigability. He had been discharged from several schools on account of his incorrigibility. The climax was reached when he appeared as a material witness in a murder trial, his evidence

being of the greatest importance in the conviction of the accused. Apart from these facts, he also complained of spasms in the muscles, especially of the calves, which occasionally awakened him by the pain caused thereby. He had frequently also had nocturnal enuresis. Upon stripping him (Fig. 184) the examination revealed the following: the body was perfectly hairless, no trace of pubic or axillary hair being evident. The genitals were small

Fig. 182.—J. M. Case I. Sella turcica small and entirely enclosed and "roofed in."

—infantile in fact—but both testicles were descended and the scrotum surrounded the penis like a labial fold. Upon eliciting the cremasteric reflex, however, the testicles were drawn up out of the scrotal sac into the inguinal canal, where they could not be palpated. He bruises very easily, the dark patch on the left raised arm being produced by the simple pressure of the examiner's thumb in raising the arm. Hands and feet are somewhat larger than they should be. Stroking the skin of the abdomen

produced a marked white line of reaction, which persisted for a rather long time. His blood-pressure was low—80 mm. Mentally he was well up to his chronologic age according to the Binet-Simon scale. Upon close questioning he admitted that he had frequent headaches referable to a point midway between the temples and deep seated.

Fig. 183.—J. M. Case I. Shows thymic enlargement.

The neurologic examination was negative. Laboratory examination showed the sugar content of the blood to be 0.070 per cent. Otherwise blood and urine were negative and the Wassermann was negative. *x*-Ray examination: The sella turcica (Fig. 185) was small and encroached upon by large clinoids; the upper thorax showed a thymus shadow.

Discussion.—This case is presumably a type of the beginning of the second stage of the syndrome. It presents many of the well-marked features of a status hypoplasticus: small sella, enlarged thymus, low blood-pressure, low blood-sugar, marked fatigability, spasmophiliac and hemophiliac attributes in addi-

Fig. 184.—F. J. Case II. Age thirteen and a half years. Shows hypoplasia of genitals and a scrotal fold surrounding base of penis. Absence of hair. Bruise on raised arm from slight pressure.

tion to the obvious externals. The mental attributes are those which we frequently see in small and enclosed sellæ turcicæ. This case is presented simply as a living present example of the early beginnings of the second stage of the syndrome.

Case III.—Private B. (Fig. 186): Age twenty years; height 6 feet 1 inch. This case was sent to the Institute by Capt.

Reed, stationed at Fort Wood, to determine whether or not the man was a malingerer. His one complaint was that of excessive fatigability after moderate exertion. As a result he could not perform the military duties required of him. His musculature and his whole bearing and appearance when stripped were that of a powerfully and symmetrically built young giant,

Fig. 185.—F. J. Case II. Pituitary fossa shut in extremely by large clinoids.

and seemed to belie his statement of rapid fatigue. His early history could not be obtained with any degree of reliability, for, coming from a mountainous district of the South, he was extremely uncommunicative. In early adolescence he was a rover, traveling over many states in divers occupations, but never steadily at any one. He did say that for the past three years he had

been rapidly and steadily growing in height, that his growth was still continuing, and with it his fatigability was increasing. Stripped, he showed a splendid make-up physically. Of note was the fact that he had practically no hair on his lip or chin, no hair in the axillæ, pubic hair of the feminine type, and rather largely developed genitals. Stroking the skin produced a white

Fig. 186.—Private B. Case III. Feminine distribution of pubic hair; large genitals; height 6 feet, 1 inch. No hair on face. Seems well proportioned.

persisting reaction. His blood-pressure was between 95 and 100 mm. systolic, 80 diastolic. Blood-sugar was 0.062 per cent. *x*-Ray examination showed a sella turcica (Fig. 187) which was extremely small, with thickened anterior and posterior clinoid processes completely roofing in the cavity. A shadow in the pineal region also was evident. The thorax showed a thymic

shadow. Neurologic examination was negative. Viscera appeared normal.

Discussion.—This young man is going through the transition period from the second to the third stage. His low blood-pressure, low blood-sugar percentage (extreme normal low limit

Fig. 187.—Private B. Case III. Complete closing in of pituitary fossa by large clinoids.

should be at least 0.075 per cent.), white skin reaction line, all go to prove his statement of fatigability. In addition, he shows a crowded pituitary fossa and a pineal shadow. We have found in the past two years in a large percentage of muscular dystrophies, pineal shadows; and in extreme cases of muscle fatigue in the

adolescent, short of dystrophy, there were shadows in the pineal region. This parallelism between the myasthenic types and early involution of the pineal gland will be the subject of a future paper. This feature of the case is an example of many similar ones. But, presumably, early pineal involution also produced his enlarged genitals. He is undergoing the rapid growth incident to the second stage of the syndrome in spite of the fact of the enlarged genitals. Some authors (especially Tandler and Gross) have maintained that the hypoplasia of the genitals accounts for the continuance of the skeletal growth. That is certainly disproved here as a universality. Upon feeding of pituitary gland this youth improved sufficiently to go back to army life. After the lapse of a few months he discontinued this feeding, and shortly thereafter returned with his old complaint of fatigability. He is again improving on treatment. No white line can now be elicited, and his blood-pressure is usually at 120 mm.

Fig. 188.—G. E. R. Case IV. Height 6 feet, 3½ inches; feminine pubic hair; no hair on face; musculature seems flabby; feminine attributes.

Case IV.—G. E. R. (Fig. 188): Age twenty-two years; height 6 feet, 3½ inches; single; stenographer. Came to the Neurological Institute complaining of loss of memory and lack of sleep; feeling stuporous and extremely fatigued. His headaches intratemporal in location. Not able to do much manual work on this account, and hence took a position as stenographer.

Is exempt from military duty, being the sole support of his mother.

Past History.—While a child he was never strong; he took a long time to develop, and on account of his ways—feminine—was always known as "sissy" to his playmates. He realized this appellation to be more or less just. Would easily cry if deprived of his way, and still does so. Always was a bed-wetter, and this weakness persisted to his nineteenth year. Realizing his fem-

Fig. 189.—G. E. R. Case IV. Sella turcica with anterior cavity eroded and a deepening of posterior fossa.

inine attributes, he endeavored to compensate for them by indulging in the most manly of sports—boxing and football. But he was too slow to amount to anything here. He gave up this conflict and sank to his own recognized level—became a stenographer. He began to get headaches at seventeen years of age, at which time his excessive growth started.

Examination.—A man powerfully set-up, 6 feet, $3\frac{1}{2}$ inches high and proportionately built (Fig. 188). No hair on face or

body except in the pubic region, where it is of feminine distribution. The scrotum also is divided above the penis into typical labial folds. He shaves once in two weeks. His appearance is really pugnacious, but is not borne out by his mental attitude. He cries when questioned about the simplest difficulties. His blood-pressure is 100 mm., systolic. He has the white line reaction of the skin, and his blood-sugar was low. The *x*-ray of the skull shows a sella in which erosion of the anterior clinoid is evident and an excavation of the posterior portion of the floor (Fig. 189). The *x*-ray of the thorax shows a possible enlargement and persistence of the thymus. Neurologic examination is negative.

Discussion.—The early history is that of a thymus state. The further progress, especially the headache concomitant with the growth, is suggestive of pituitary enlargement. This is partly borne out by the picture of the sella. His headaches are now much less prominent than they were, but his fatigability is marked. His growth seems to have ceased. This case belongs in the third stage—with the giantism gradually reaching its acme, with the stuporous and drowsy mental condition of a dyspituitaric still present, great fatigability, low blood-pressure, and low blood-sugar content. The enlargement of the sella turcica, however, gives promise of a gradual efficient compensation taking place. Feeding of whole gland pituitary extract within two weeks measurably improved all his symptoms. It is still being continued.

Case V.—W. W., thirty-two years; machinist; married; several children; height 6 feet, 4½ inches; acromegaly in slight degree. This case has been under our observation since 1912. At first the complaint was one of utter exhaustion to the exclusion of all minor ills. He could not stand at his work, he could hardly walk without becoming exhausted. At nineteen he had severe headaches referred to the intratemporal region, which persisted in spite of all measures. These headaches he described as "crushing." At the same time his hands enlarged while under our observation. The fatigability was so great that he would have to take to his bed and remain there. His past history was typical of the thymic. Nosebleeds, general weakness, enuresis,

overextensibility of the joints. His family history was a typically endocrine one. On his mother's side four members of direct and collateral branches had goiter, two with exophthalmos. His father never shaved until the age of twenty-eight. Puberty in this patient was reached at nineteen. Hairy growth in the axilla and on the face remained absent. To this day he has never shaved. During the period of intense headaches and growth he had various vagotonic symptoms; hyperacidity; excessive perspiration; precordial distress; nausea and vomiting; marked pallor; lack of libido. His gastric distress became so acute that operation was advised at another hospital for gastric ulcer. At this time an *x*-ray of the skull was taken and showed a large sella turcica, with practically no clinoids present at all, and erosion at the edges. His photograph (Fig. 190) has some interesting points. The extreme length of leg compared with thorax is noteworthy. The feminine distribution of pubic hair and feminine waist are present. His extremely large hands and generally deficient musculature attract notice. This photograph was taken about a year ago when he was just completing his cure. Today he has gained 30 pounds in weight and is feeling practically well, working constantly as machinist, and supporting his family of wife and two children. During the last three years his blood-pressure had gradually risen to 130 mm. systolic from an initial

Fig. 190.—W. W. Case V. · 6 feet, 4½ inches. Fully compensated case. Great length of leg compared with length of thorax. Feminine waist; feminine pubic hair; acromegalic hands; no hair on face.

90 to 100 systolic; his gastric symptoms have abated, the white line of adrenal deficiency is diappearing; his fatigability has passed; libido has returned, and he is, to all purposes, cured of his malady. His fatigability and headaches in the past three years could always be improved with the administration of whole gland pituitary extract, and gradually it became possible to diminish the dose and to allow the compensation to proceed unaided. He has now been without treatment for practically six months. He seems to be a fully compensated case.

Discussion.—The history and progress of this case is typical of all cases passing through the complete syndrome, and is presented as a type of which I have now seen at least ten examples. It must not be forgotten that he now shows giantism plus acromegaly. That does not mean that his clinical picture indicates treatment. Far from it. Hs is a finished case. The giantism and acromegaly are incidents merely of the compensatory process—they themselves do not necessarily indicate present disease. This is a point well worth remembering. Many cases showing endocrinopathic features come under our notice, and it should be our first aim to determine whether or not they represent processes that have come to a stop through compensatory efforts of which they are the indices. Under such conditions, of course, no treatment is called for. An interesting case of this nature was seen at Mt. Sinai Hospital, New York, in the service of Dr. Goldenberg, through the kindness of Dr. I. Strauss. A woman, fifty-three years of age, with typical acromegaly—hands, feet, and skull abnormalities—was admitted for some minor ailment. Her history showed that she began to menstruate at nineteen years, had intense headaches at twenty-five years, which for three years resisted all attempts to alleviate, and during whose persistence she began to grow acromegalic. When the headaches spontaneously ceased the abnormal growth ceased, and she passed an uneventful life to the time of the present slight ailment. Her childhood and adolescence were like those described in the first two stages of this syndrome—fatigability being the prominent symptom. Her acromegaly then was completed at about the twenty-ninth year, did not further increase, and she remained

well for twenty-three years longer. This was also a "finished" case as far as the syndrome of thymus, adrenal, and pituitary was concerned. This case might be many times duplicated.

UNCOMPENSATED CASES

I desire to give rapidly the salient features only of several uncompensated cases belonging to the syndrome:

Fig. 191.—J. S. Uncompensated Case 186. Shows pituitary fossa completely enclosed. Stereoscopic plates confirm this. Age twenty-two years; height 6 feet.

Case VI.—Miss J. S. Referred by Dr. Robert T. Morris. Height 6 feet, large hands and feet, extreme fatigability, headaches, vagotonia, rapid growth in past two years, with a past history of status thymicolymphaticus; comes for relief of her headaches and fatigability. Blood-pressure 95 systolic; blood-sugar 0.065 per cent.; fatigue so great that she must remain prone the greater part of the day. Intense white line. Her sella turcica

(Fig. 191) shows a roofing in by the clinoids. Pituitary feeding gave gratifying results, but must be continuously carried out.

CASE VII.—T. R. Age thirty-five years; height 6 feet, 1 inch. Obese (220 pounds). Early fatigability. Late puberty. Feminine pubic hair. Unmoral. Intense intratemporal headaches. Although wealthy, and of excellent family, commits sexual and other excesses. Frequently in jail. Fatigability and

Fig. 192.—T. R. Uncompensated Case 187. Age thirty-five years; height 6 feet, 1 inch. Sella turcica completely shut in and extremely small. Confirmed by stereoscopic plates.

headaches persist. With beginning of headaches growth began. Blood-pressure 95 mm. Sella turcica small and closed in by the clinoids (Fig. 192); polyuria. Pituitary feeding helped not only his headaches and fatigability, but strangely and unexpectedly his moral sense is elevated and his excesses are no longer indulged in. But the pituitary feeding must be constantly kept up. A few weeks of discontinuance leads rapidly to the old condition. He has been now practically free of his trouble for two years.

CONCLUSION

The syndrome of thymus—adrenal—pituitary combination is one frequently met with, and its various stages are easy of recognition. The main characteristics of fatigability—low pressure, headache, and growth—are invariable components of the syndrome, and depend upon maladjustments of endocrine interactivity. Stabilization of the balance may be spontaneously produced providing the sella turcica may be made to accommodate a hyperactive hyperplastic pituitary gland. This is done presumably by erosion of the bony capsule of the gland. In cases of inability of such enlargement of the sella, the syndrome persists, but the symptoms may be alleviated by the feeding of pituitary extract continuously. In the course of the syndrome other glands may be brought into the complex and alter the picture somewhat, but these are vagaries and seemingly have no great determining effect upon the course of events. Once recognized in any of the early stages, the further general progress of these cases can be prognosticated with a great degree of accuracy; and intervention, if necessary, can be undertaken with a large degree of success in the amelioration of the distressing symptoms.

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CLINIC OF DR. WALTER W. PALMER

PRESBYTERIAN HOSPITAL

PNEUMOCOCCUS ENDOCARDITIS

Acute Endocarditis Occurring in Course of Acute Lobar Pneumonia Treated with Antipneumococcus Serum; Early Diagnosis; Care in Administration of Serum.

March, 1919.

CERTAIN interesting features in the course of the use of antipneumococcus serum in the treatment of acute lobar pneumonia have come to light in the past few weeks, and I wish to present 3 illustrative cases. All of you are now familiar with the biologic classification of the pneumococcus and the importance of this differentiation in the prognosis and treatment of the disease. It might not be out of place for you to read again the clinic by Dr. Rufus Cole which appeared in the New York number of the Medical Clinics of North America, November, 1917. Dr. Cole describes in detail the manner in which the various types are determined, and also points out that antipneumococcus serum has proved of value in the treatment of cases infected with Type No. I pneumococcus. The administration of foreign serum, such as horse-serum, to human individuals must be performed with certain precautions to avoid the production of anaphylactic shock, which at times is fatal. Great emphasis is placed on the manner in which serum should be given. It is not the purpose of this clinic to discuss these details, nor do I propose to dwell on the subject of the general treatment of pneumonia. We will now proceed to a presentation and discussion of the cases.

CASE I (Chart I, Hospital No. 37,461).—J. M., aged twenty-eight, Spanish cigarmaker, entered the hospital for the first

time February 27, 1918, complaining of pain in left side, fever, and general malaise of six days' duration. His family and past history contain nothing relevant to the present illness (Fig. 193).

Six days ago the patient was seized suddenly with a sharp pain in left chest, followed by a chill, which in turn was followed by fever and cough, causing him to take to bed. In twenty hours he felt much better and got up. Five days later, or twenty-four hours ago, he was seized suddenly with a second chill, pain

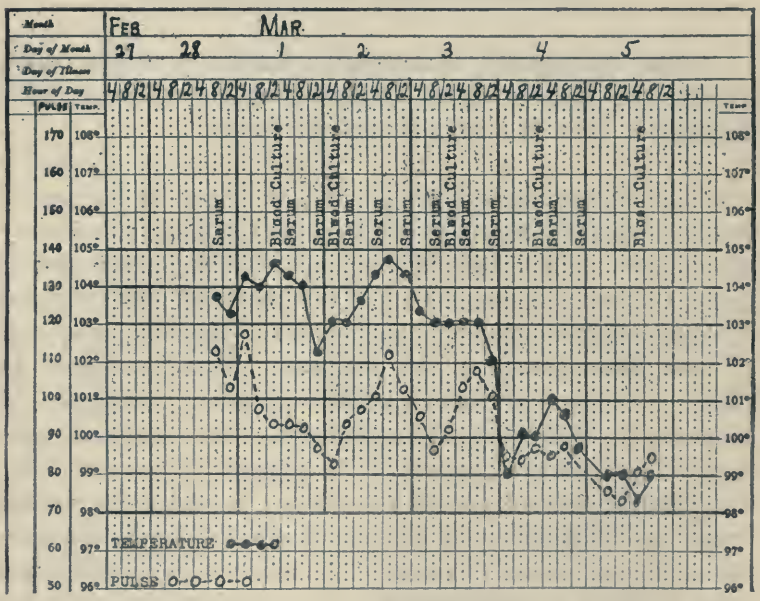

Fig. 193.—Chart of Case I.

in the left chest, and was nauseated. Following the chill he became feverish, much prostrated, a severe headache developed, and he began to cough up bloody sputum. Deep breathing and cough produced much pain in the left chest.

The physical examination presents little of especial interest except in the left lung posteriorly, where from the lower angle of the scapula to the base there is dulness, increased voice whisper, a few crepitant râles, and friction-rub. W. B. C. 12,000; 87 per cent. polynuclears. Urine showed nothing abnormal.

No difficulty presents in making the diagnosis of acute lobar pneumonia. It is of interest to pause a moment on the history. Are we dealing with a one-day- or a six-day-old pneumonia? The history is very suggestive of a one-day pneumonia, occurring six days ago, with a more definite and severe attack twenty-four hours ago. As it is not possible to be sure on this point, we shall have to leave it an open question.

On the day of his admission, as usual, the sputum was sent to the laboratory, but through some error the typing was delayed, and it was not until the second day after admission when the blood-culture revealed a Type I pneumococcus, 1–2 colonies per c.c., that the type of infection was known. The same day a Type I pneumococcus was obtained from the peritoneal washings and heart's blood of a mouse which had been injected with the patient's sputum. At this point let me emphasize the great importance of determining the type of pneumococcus at the earliest possible date. I could present case after case where serum has apparently shortened the disease by several days. In certain of the cases of lobar pneumonia occurring among the hospital staff the diagnosis of type has been made, the patient desensitized, and serum given within twenty-four hours after the initial chill; and I have seen the temperature come to normal after one intravenous treatment of antipneumococcic serum.

February 28th: The usual intracutaneous injection of 0.02 c.c. of a 1 : 10 dilution of normal horse-serum was made without evidences of hypersensitiveness. One hour after this test was performed the customary ½ c.c. of horse-serum to desensitize the patient was injected subcutaneously. Within ten minutes the patient became moderately dyspneic and restless for a period of about one minute. One hour and a half later preparation for injection of the usual 100 c.c. of antipneumococcus serum Type I was made. About 1 c.c. of the serum was injected, taking about five minutes, when suddenly the patient began to cough violently, sitting up in bed, with a severe choking sensation. The injection of serum was immediately stopped, and 10 minims of adrenalin solution, 1 : 1000, injected subcutaneously, with almost immediate relief. If any of you in the future contemplate the

use of serum intravenously, I trust you will keep well in mind the above incident. The symptoms following the injection of ½ c.c. of horse-serum subcutaneously should have been a warning of the sensitiveness of the patient, and the desensitization process so carefully described by Dr. Cole and co-workers resorted to. In this instance enough serum has been given apparently to accomplish this, for the day following we note:

March 1st, 1.30 P. M.: "2 c.c. of half horse-serum and half saline was injected intravenously. No reaction. Injected very slowly with adrenalin at hand."

2.15 P. M.: 90 c.c. antipneumococcus serum injected intravenously. No reaction.

Before the intravenous serum of this day a blood-culture was taken, showing an average of 900–1000 colonies of Type I pneumococcus per cubic centimeter.

	11.00 P. M.:	100 c.c. antipneumococcus serum intravenously.
March 2d,	9.00 A. M.:	100 c.c. antipneumococcus serum intravenously.
	5.00 P. M.:	Blood-culture—sterile.
	6.00 P. M.:	100 c.c. antipneumococcus serum intravenously.
March 3d,	12.30 A. M.:	100 c.c. antipneumococcus serum intravenously.
	10.30 A. M.:	100 c.c. antipneumococcus serum intravenously.
	4.00 P. M.:	Blood-culture—sterile.
	4.45 P. M.:	100 c.c. antipneumococcus serum intravenously.
March 4th,	12.30 A. M.:	100 c.c. antipneumococcus serum intravenously.
		Blood-culture—sterile.
	2.30 P. M.:	100 c.c. antipneumococcus serum intravenously.
March 5th:		Blood-culture—sterile.
March 8th:		Serum sickness.

The patient made an uneventful recovery, with no extension of the process after the initiation of the serum treatment.

Two important facts are strikingly illustrated by this case: (1) Great care must be exercised in the administration of antipneumococcus serum; (2) serum sterilizes the blood in an uncomplicated case. It is necessary to draw conclusions with great conservatism, but we cannot help but be impressed by the fact that on the day of entrance there was only one to two colonies per cubic centimeter of blood, and two days later the bacteria had increased to 900 to 1000 colonies per cubic centimeter of blood.

We know from considerable clinical experience that an increase in the bacteriemia in pneumonias is of bad prognostic omen. In fact, a bacteriemia of over 100 colonies per cubic centimeter carries with it a definite bad prognosis in the average case. The prompt sterilization of the blood by the administration of antipneumococcus serum is certainly convincing evidence of its value in cases such as the one under discussion.

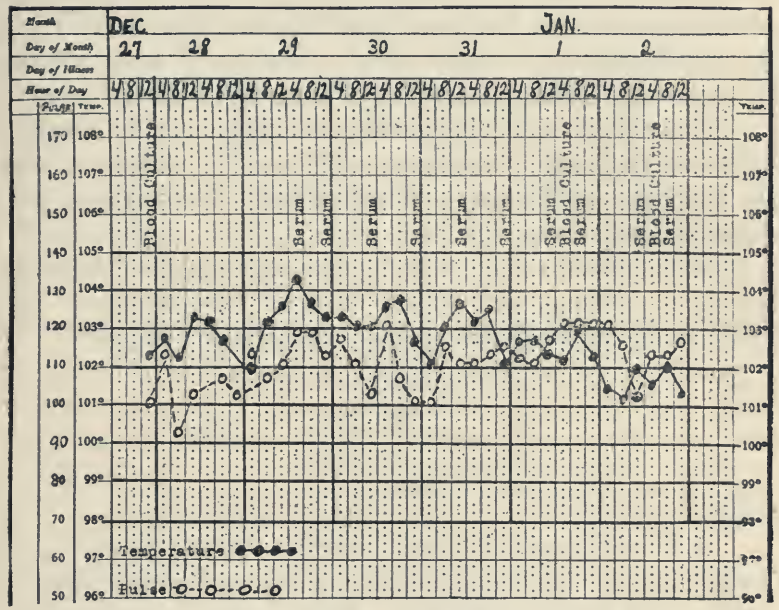

Fig. 194.—Chart of Case II.

CASE II (Chart II, Hospital No. 36,934).—G. H., an American printer, aged fifty-five, entered the hospital December 27, 1917, for the first time, complaining of pain in the right side, difficulty in breathing, and general weakness of five days' duration. His father and mother both died of pulmonary tuberculosis. The patient is subject to colds, with hoarseness and cough, frequently requiring a day or two in bed, but has never had pneumonia. Never had rheumatism; denies syphilis (Fig. 194).

Five days ago, quite suddenly, felt chilly and much prostrated, immediately taking to bed. The day following there appeared in the right lower axilla pain, which was increased on cough and deep breath. He began to cough and raise bloody sputum. Both cough and pain have persisted, and for the past two days there has been difficulty in breathing.

The patient is a poorly nourished old man, lying quietly in bed, cyanotic, breathing rapidly and with difficulty. There is extensive herpes of the upper lip. The left side of the chest moves with greater excursion than the right on deep inspiration. On the right side, from the lower angle of the scapula to the base, there is dulness, diminished tactile fremitus, bronchial breathing and voice, with many crepitant râles. At the base in the posterior axillary line is a friction-rub. The left lung presents no adventitious signs.

Heart: Apex-beat not seen or felt. No thrills. The heart sounds are regular and of fair quality. No murmurs. The aortic second sound is accentuated. Percussion outlines:

1— 2.5
2.5—2— 5
4—3— 7
5—4— 9
5—10.5

The pusles are equal and regular; good volume and tension. Artery walls slightly thickened. White count, 15,700; 90 per cent. polynuclears.

The urine is amber colored; specific gravity 1018, containing a trace of albumin, many hyaline and granular casts.

As in the previous case, we experience no difficulty in the clinical diagnosis—that of acute lobar pneumonia. I have given the physical signs of the heart as found at entrance because of subsequent developments. There is no evidence of valvular disease nor has the patient had rheumatism. During life syphilis was not ruled out. Although it is a custom of the clinic to have a Wassermann test on all admissions, for some reason it was omitted in this case. It was later demonstrated

that there was no syphilitic infection of the heart valves. The blood-culture taken on the day of admission revealed a Type I pneumococcus in both broth flasks. As in all individuals with lobar pneumonias who enter this hospital, the patient was tested for horse-serum sensitiveness by the intracutaneous injection of 0.02 c.c. of horse-serum diluted to 1 : 10. As no reaction followed this procedure, a desensitizing dose of ½ c.c. of horse-serum was injected subcutaneously, also without reaction.

At 6.00 P. M., December 29, 100 c.c. of antipneumococcus serum Type I was injected intravenously. Blood-plates made just before the serum was injected revealed 3 to 5 colonies per cubic centimeter. It has been found from considerable experience that such serum administration invariably sterilizes the blood after a single injection—unless, however, there are complications. Keeping this fact in mind, the subsequent record will be of interest:

December 30th, 12.15 A. M.: Blood-plates showed 35 colonies per cubic centimeter Type I pneumococcus.
100 c.c. antipneumococcus serum Type I given intravenously.
12.00 M.: Blood-cultures just before serum administration grew Type I pneumococcus.
100 c.c. antipneumococcus serum intravenously.
10.00 P. M.: 100 c.c. antipneumococcus serum intravenously.
December 31st, 12.00 M.: Blood-culture, Type I pneumococcus.
100 c.c. antipneumococcus serum intravenously.
10.00 P. M.: 100 c.c. antipneumococcus serum intravenously.

The process in the lungs remains about as at entrance. There is no evidence of a spread discovered. The patient's general condition is fair.

1918.
January 1st, 12.00 M.: Blood-culture pneumococcus Type I.
100 c.c. antipneumococcus serum intravenously.
4.00 P. M.: Blood-culture—contaminated.
9.00 P. M.: 100 c.c. antipneumococcus serum intravenously.
January 2d, 2.00 P. M.: Blood-culture, pneumococcus Type I, 2 colonies per cubic centimeter.
100 c.c. antipneumococcus serum intravenously.
9.00 P. M.: 100 c.c. antipneumococcus serum intravenously.

The patient appears slightly better this morning. Pulse good, and temperature by rectum 100.8° F. Signs of resolution are to be made out over the process in the right upper lobe. Posteriorly on the left from the lowest angle of the scapula extending downward and toward the spinal column there is dulness, bronchial breathing, and crepitant râles.

White blood count, 22.600; polynuclears, 96 per cent.

In view of the fact that the patient has had a liter of antipneumococcus serum without apparent benefit, further use of serum seems unwise. The heart examination reveals no evidence of endocarditis.

January 7th: Blood-culture, pneumococcus Type I.
Heart sounds fair quality; a soft systolic murmur at apex is heard.

January 8th: The patient visited at 9.45 A. M. Was quiet, apparently sleeping. When seen two hours later the breathing stertorous, ptosis of the left eyelid, right side of face smooth, with the left corner of the mouth drawn to the left, and great weakness of the right arm and leg. This condition persisted, and patient became more and more stuporous, pulse and temperature rising, dying in the early morning of January 10th.

When the serum failed to clear the blood of pneumococci, some complication was immediately suspected. The particular type of complication most likely to cause a bacteriemia to persist is, of course, an endocarditis, and this was suspected before any change in the physical signs of the heart occurred. Other complications were, of course, sought. There was no evidence of abscess, empyema, meningitis, or pericarditis. On the 7th of January a systolic murmur appeared, but while this is very suggestive, it is not conclusive, for patients very ill for days may develop a functional cardiac murmur. On January 8th, however, additional evidence appeared in the sudden appearance of a hemiplegia. Here again this could be due to cerebral hemorrhage, but with the persistence of the bacteriemia and the development of the cardiac murmur we were strongly inclined to believe this phenomena to be due to an embolus. Evidence of other emboli was sought for, but not found.

Autopsy: Lobar pneumonia involving the entire right upper and posterior portions of lobe, posterior half of left upper, and entire left lower lobe; acute fibrinous pleurisy, most marked at the right base; abscess in apex of right lung (a cavity measuring about 3 cm. in diameter); acute splenic tumor, small infarcts in spleen; parenchymatous degeneration of the liver and kidneys; chronic pancreatitis, fat necrosis in the pancreas; and acute vegetative endocarditis of the mitral valve (pneumococcus).

Heart weighs 350 grams.

MEASUREMENTS

Pulmonary valve	Normal.
Tricuspid valve	Admits three fingers.
Mitral valve	Admits two fingers.
Aortic valve	Normal.
Thickness of right ventricle	0.3 cm. in thickness.
Thickness of left ventricle	1.6 cm. in thickness.

The pericardial surface is smooth and shining, pericardial fat slight in amount. All chambers of the heart are filled with postmortem clot; no thrombi present. All of the valve cusps are normal except the mitral. On the auricular surface of both mitral leaflets there are four vegetations about equal distance apart, attached about the line of closure. Two of the vegetations are rather large, measuring approximately 0.5 cm. in height and perhaps 2 mm. in width. They are opaque, grayish-white in color, and look firm, as though organized. About their bases they can, however, be crushed readily, and obviously are recent in origin and composed almost entirely of fibrin and platelets. There is no evidence of an old valvular lesion. There are no vegetations on the auricular wall or on the chordæ anywhere. The cardiac musculature is pale, but otherwise normal.

Smears taken from the abscess in the lung and the heart vegetations revealed Gram-positive, lancet-shaped diplococci with capsules present—large numbers. Unfortunately, the cultures failed to grow.

To make this case complete, a head examination should

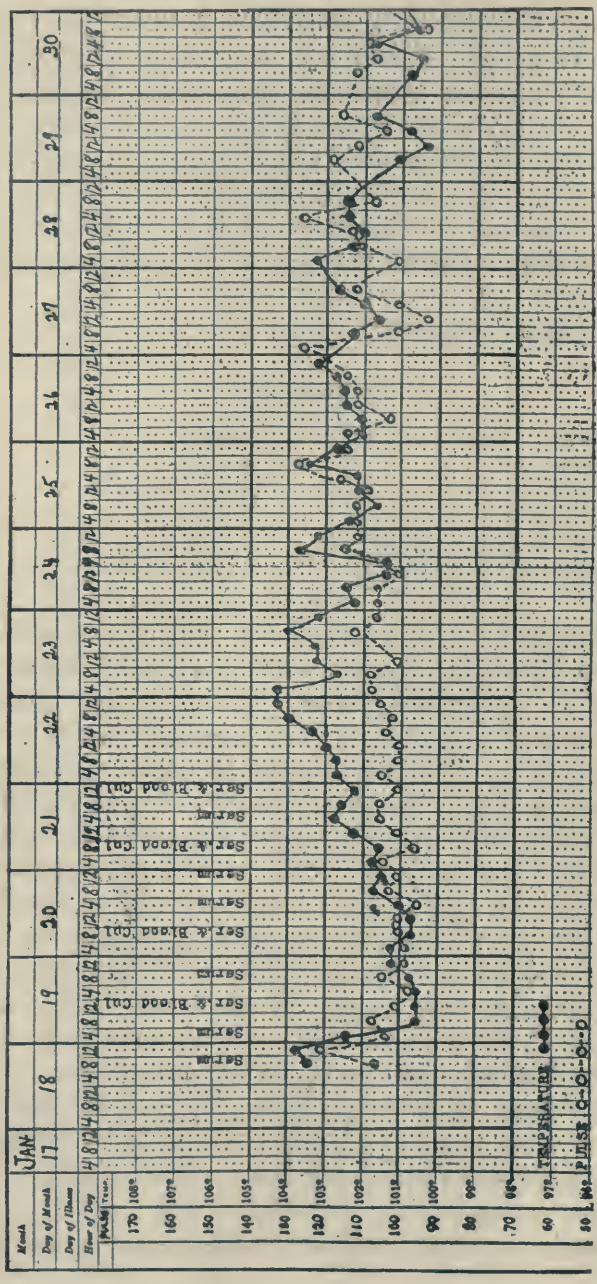

Fig. 195.—Chart of Case III.

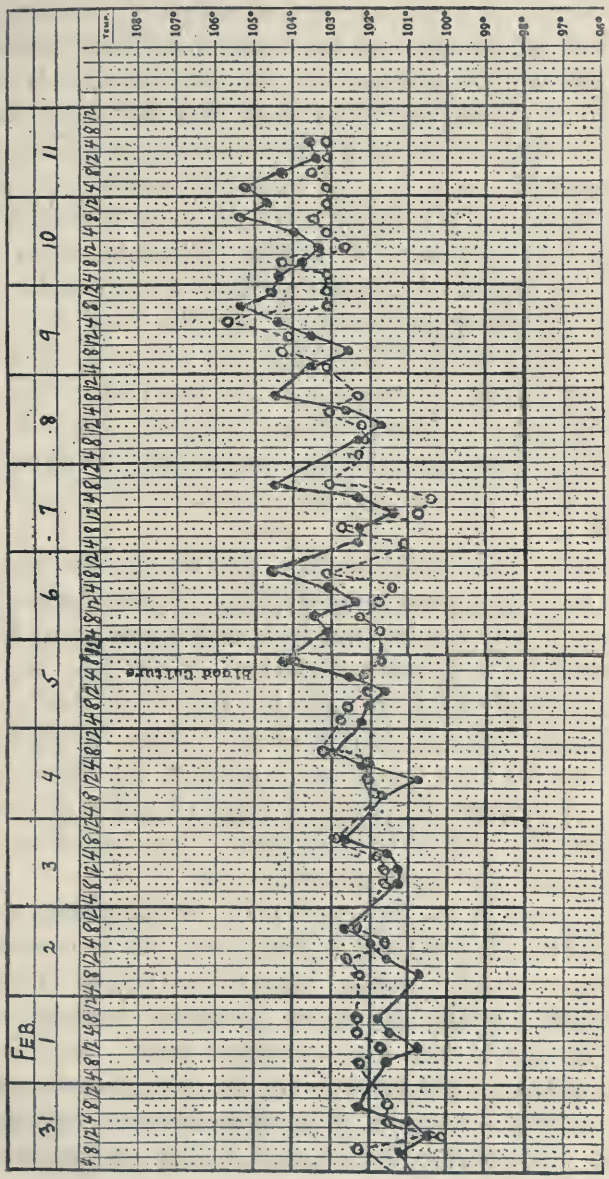

Fig. 196.—Chart of Case III (continued).

have been made, and it is to be regretted that this was not allowed.

You will undoubtedly ask the question, Did not the abscess play a part in the persistence of the bacteriemia? It is impossible to say dogmatically that it did not, but it is a matter of common clinical knowledge that abscesses following pneumonia frequently occur without an accompanying bacteriemia.

Case III (Chart III, Hospital No. 37,109).—A negress, aged thirty-five, laundress, born in Georgia, entered the hospital for the first time January 17, 1918, complaining of weakness and a "bad cold" of ten days' duration. She has been married for five years, has one child four years old and well. One child died at four months of pneumonia, and two miscarriages "one week before term." She has always considered herself well and strong. Five years ago she had pneumonia associated with jaundice. One year ago, sore on vulva followed by rash (Figs. 195, 196).

Ten days before entrance the patient got her feet wet. The next morning she was suddenly seized with violent headache, which very shortly was followed by a severe chill, which in turn was followed by fever and prostration. A day later the headache disappeared and there appeared in her left side a severe knife-like pain, which was made worse by deep breathing and cough. She has been much prostrated with the fever, pain in the side, and cough since onset. The day before she entered the hospital she noticed that her fingers were yellow and that her urine was a very light yellowish color.

The patient is a well-developed, well-nourished colored woman, acutely ill, breathing rapidly, apparently in considerable discomfort. Frequent cough. Scleræ are yellow. Over the left lower lobe posteriorly there is dulness, bronchial voice, and breath sounds with many crepitant râles.

Examination of the heart: The apex-beat is not seen nor felt. No thrills. The area of cardiac dulness is only slightly increased. The sounds are of good quality and no murmurs are heard. The aortic second is not accentuated.

The diagnosis of the acute condition in this case, of course,

presents very little difficulty. Both history and physical examination are typical of lobar pneumonia. The history of miscarriage and sore on vulva would lead us to suspect syphilis. As we stated at the outset, we shall spend little time on the disease pneumonia, but dwell rather on the special features of the case in connection with the heart.

January 18th:		W. B. C., 25,000; 88 per cent. polynuclears. Urine orange colored; 1025, acid; albumin, a heavy trace. Few granular casts; bile present. Sputum, pneumococcus, Type I. Blood-culture, pneumococcus, Type I. Wassermann; alcoholic antigen, ++++; cholesterin, ++++.
	4.00 P. M.:	½ c.c. of Wassermann injected subcutaneously was followed by no reaction.
	8.00 P. M.:	100 c.c. antipneumococcus, Type I, intravenously.
January 19th:	12.00 M.:	Blood-culture, Type I pneumococcus. 100 c.c. antipneumococcus serum, Type I, intravenously.
	8.00 P. M.:	100 c.c. antipneumococcus serum, Type I, intravenously.
January 20th:	9.00 A. M.:	Blood-culture, Type I, pneumococcus.
	9.00 A. M.:	100 c.c. antipneumococcus, Type I, intravenously.
	4.00 P. M.:	100 c.c. antipneumococcus, Type I, intravenously.
	12.00 P. M.:	100 c.c. antipneumococcus, Type I, intravenously. Note on this day is that patient is much more comfortable and jaundice much less marked.
January 21st:		W. B. C., 36,000.
	9.00 A. M.:	Blood-culture, Type I pneumococcus. 100 c.c. antipneumococcus serum, Type I, intravenously.
	4.00 P. M.:	100 c.c. antipneumococcus serum, Type I, intravenously.
	12.00 P. M.:	100 c.c. antipneumococcus serum, Type I, intravenously.

Blood-culture taken just before the midnight dose of serum showed Type I pneumococcus.

For the first time, on January 21st, a systolic murmur at the apex was noted. The lung signs up to this time revealed no evidence of any spread of the process, nor was there any reason to think the affected lobe was breaking down with abscess formation. There were no signs of meningeal involvement.

Up to this point the striking feature of the case was the fact that after the first dose of the serum the blood still contained the type of pneumococcus which in the light of Case II, particularly without other obvious complications, suggests immediately a pneumococcus endocarditis. No cardiac murmur could be made out at this time. Subsequent serum treatments failed to clear the blood of this type of pneumococci. The patient had in all 900 c.c. of antipneumococcus serum. This is a very large amount when we consider that in the successfully serum treated cases of Type I infections require on the average of only 200 to 300 c.c. of serum. With the development of the murmur on January 21st our suspicion of an endocarditis received very convincing support. Further events bear out our early ideas of the situation:

January 25th: Signs of resolution (many moist râles, decrease in dulness and bronchial character of the voice and respiration) are present at the extreme base of the lung. Apex murmur remains about the same as on January 21st

January 28th: Blood-culture: Pneumococcus, Type I, present.

January 31st: Lung signs rapidly clearing up.

February 4th: Roentgenograms reveal no disease of the lungs.

February 5th: The systolic murmur at the apex is louder and harsher than when last noted. Just along the left sternal margin in the second and third interspaces is heard a short soft diastolic murmur. A capillary pulse is present in lips and fingers.

Blood-culture: Pneumococcus, Type I; average number of colonies per cubic centimeter, 31.

Note.—Patient's family suddenly decided to take the patient home on February 11th. The visiting nurse reported that the patient died four days after leaving the hospital.

While we have no autopsy in this case, the clinical evidence is very conclusive that we are dealing with a case of acute pneumococcus endocarditis developing during the course of acute lobar pneumonia. In this case there is the presence of syphilis, which may have been a predisposing factor. We know that acute endocarditis of this type is more prone to develop on valves which have been previously diseased, as in old rheumatic endocarditis and syphilitic endocarditis. No

evidence that there was an old syphilitic endocarditis is present. That is a possibility, however, but not a very great one.

In conclusion, we may call attention to the fact that acute pneumococcus endocarditis may be diagnosed with some certainty in the Type I pneumococcus pneumonia before cardiac signs appear. This is of importance from a prognostic standpoint.

CLINIC OF DR. T. STUART HART

Presbyterian Hospital

MITRAL STENOSIS AND AURICULAR FIBRILLATION. DIGITALIS—ITS USES AND DANGERS

This afternoon, gentlemen, I wish to discuss with you not a rare, not a spectacular condition, but an exceedingly common one, a condition which each one of you will meet frequently in your practice, namely, *mitral stenosis* associated with *auricular fibrillation*. Although these cases are occasionally puzzling, their diagnosis usually presents but little difficulty. The treatment of many of them is most satisafactory, but in order to secure satisfactory results each patient must be individually considered; they need constant supervision, and the details of their treatment must be modified from time to time as the special indications develop. It is this question of individualization to which I wish to especially invite your attention.

Case I.—The first patient which I wish to present for your consideration is a man sixty-one years of age whom I have asked to give up his work for the afternoon and to come before you because he represents in a most interesting manner a sequence of events to which I wish to direct your attention.

As a child he had a severe attack of scarlet fever. Following this he had several attacks of tonsillitis, and at nineteen years of age a Neisserian infection. With the exception of these illnesses he was perfectly well. He has never had acute rheumatic fever. He denies luetic infection. He has used alcohol moderately, never to excess. He has never used tobacco. When twenty-three years of age, while occupying a clerical position which he has continued ever since, it was accidentally discovered that he had a heart murmur. At this time he had no subjective symp-

toms, but was told that he had a valvular lesion and was advised to avoid excessive physical exertion. He has accordingly always led a quiet life, keeping in mind the possible danger from his valvular defect and avoiding any considerable bodily activity. The first subjective symptoms which appeared were twenty years later when he was forty-three years of age. Up to this time he had been perfectly well and had no symptoms referable to his heart. He then began to notice that occasionally he had a sensation of "thumping" in the precordial region, and discovered that his heart was irregular. Beyond this, however, he suffered no inconvenience, but continued his quiet mode of life, at this time attributing these occasional attacks of irregularity to gastro-intestinal disturbances.

He first came under my observation in 1909 when he was fifty-one years of age. At that time there was nothing in his physical examination that was abnormal except the condition of the heart, which showed the following features: The apex was palpable in the fourth space 9 cm. to the left of the midsternal line, dulness 10 cm. to the left of the midsternal line, none to the right of the sternum. No thrills could be detected. The first sound at the apex was snappy and was preceded by a rough crescendo murmur, terminating abruptly in the first sound. Along the left edge of the sternum with maximum intensity in the third space was heard a loud diastolic murmur. The sounds at the base of the heart were normal. During the period of the examination occasional extrasystoles were detected. At this time there was no evidence of cardiac insufficiency. In January, 1911, he developed an attack of bronchopneumonia. At the onset of this attack the heart showed no changes from the condition which I have described to you, but during the course of this disease the heart became suddenly very irregular and increased somewhat in size, but not to any considerable degree. He was given digitalis. The heart rate was gradually controlled and he made a satisfactory recovery from his pneumonia. He was discharged with the advice to limit his physical activities and to continue taking digitalis. The latter, however, he neglected to do, and in the latter part of April of this same year he

presented himself complaining of a moderate degree of dyspnea on slight exertion and slight pretibial edema. His heart showed complete irregularity, a rate counted at the apex of 132 and a radial pulse of 104. The heart apex was farther down and more to the left than on former examinations. It was located in the fifth space 11 cm. to the left of the midsternal line. He was at once put to bed and given effective doses of digitalis. In two weeks the heart rate was reduced to 81 per minute, the radial rate was 74 per minute. He was then allowed to leave his bed and to gradually resume his office work. His greatest desire at that time was to be able to continue his work, upon which the support of his family depended. He was, therefore, instructed to save his physical exertion in every possible way. He accomplished this by never climbing stairs, by using the surface cars rather than the subway or elevated, by returning home as soon as his work was completed and going immediately to bed, staying there until it was time for him to get up and return to his office the next morning. After a time these restrictions were made less rigid, and at the present time he is able to lead a fairly normal life as to hours, but his physical activities are always limited. During this whole period he has never failed to take his daily dose of digitalis in amounts which I have found were suited to his individual necessities. At the present time his heart shows complete irregularity. The apex is in the fifth space 13 cm. to the left of the midsternal line. The presystolic and the diastolic murmurs are still present and, in addition, there has developed a loud systolic murmur heard with maximum intensity at the apex. The lungs are clear. The liver is palpable 2 cm. below the costal margin. There is no edema of the extremities. His color is good. There is no dyspnea on the exertion to which he is accustomed.

It is evident that we are dealing with a case of chronic cardiac valvular disease. Let us briefly review the history together, considering *first* the cause of the valvular defect, *second*, the anatomic condition, and *third*, the changes in the functional activity of the heart. In his story we have an account of three infections—scarlet fever, repeated tonsillitis, and gonorrhea.

It is impossible to say which one of these infections was the cause of the cardiac condition, but it is most probable that the scarlet fever afforded the infection which began to deform the heart valves.

It is clear from the evidence that his early valvular defect was a mitral stenosis. The mitral valve evidently became more and more deformed until at the present time it is clear that he has a mitral insufficiency as well as a stenosis. Hand in hand with the changes in the valves has developed a change in the heart muscle. At first there was little or no change in the size of the heart. At the present time there is evidence of a considerable hypertrophy of the left ventricle. This, of course, is nature's method of adjusting the heart to meet the conditions arising from the valvular defect. The ventricle is thus strengthened and is better able to maintain the circulation.

The first symptom of which this patient was conscious was a "thumping of the heart," and this, he himself discovered, was due to irregularity in its action. As this irregularity was present when he first came under my observation I can describe to you its features as I found them when I made the examination. When I felt the pulse at this time I found that for considerable periods it was perfectly rhythmic, with good sized pulse waves following each other in normal succession, then there would appear a small wave which occurred a little too early and which was barely palpable. This was followed by a pause which was longer than the interval between two of the rhythmic pulse waves. The pause, in turn, was followed by a large wave, and then there was a succession of regular rhythmic pulse waves. When one auscultated the heart a similar sequence of events was evident. For the most part the heart was perfectly rhythmic, but occasionally there was a beat which occurred a little too early; this was followed by a pause and then the rhythmic series was continued. You will thus recognize this as a description of an extrasystole, as you know the extrasystole is due to a contraction of the heart the stimulus for which arises from some portion of the heart muscle other than the sinus node where the impulses normally originate. Some portion of the heart muscle becomes

irritable and initiates a contraction before the time that the normal contraction which arises at the sinus node appears. The next impulse coming from the sinus node finds the heart muscle exhausted and unable to respond to this stimulus, that is, the heart muscle is in its "refractory period," hence it does not contract, and there is a pause which permits it to recover, and it is ready to respond to the next physiologic stimulus coming down from the sinus node.

The sensation of "thumping" is a common description given by the patient to this form of irregularity. His sensation is due to the fact that the contraction does not pass over the heart muscle by the normal path, and therefore is ineffectual in emptying the ventricles, giving rise to this abnormal sensation in the chest. You will notice that notwithstanding the easily recognized valvular defect, the change in the size of the heart and the presence of extrasystoles, that this patient developed no symptoms of cardiac insufficiency for a period of over thirty years.

Eight years ago he had an attack of pneumonia. During this time the heart became completely irregular and symptoms of insufficiency first developed. By complete irregularity we mean a heart activity in which we cannot predict what the next event is to be. Heart-beats follow each other in irregular succession without rhyme or reason. We have a series of contractions following each other in rapid succession, and these are separated by long or short intervals. The time relations and volume of the successive waves of the pulse are correspondingly irregular, and we have a haphazard succession of large and small waves separated by longer or shorter intervals which occur in utter confusion. There are several conditions which may give rise to complete irregularity of the heart action. Only one or two of these, however, need arrest our attention. By far the most frequent cause of complete irregularity is the condition known as (1) fibrillation of the auricles. Other conditions which one should bear in mind are (2) a sinus arhythmia in which the normal pace-maker at the sinus node loses its usual rhythmicity, but still retains its function as pace-maker of the heart, and (3) the very frequent occurrence of extrasystoles at irregular intervals so dis-

torting the normal rhythm that it gives one the impression of complete irregularity. Auricular fibrillation, however, is by far the most frequent cause of complete irregularity, and it is the cause of this type of activity in at least 95 cases out of every 100. We may obtain corroboration of this condition by inspecting the veins of the neck when their pulsation is prominent enough to give us satisfactory information. When the auricles are fibrillating there is no presystolic wave to be detected and all the venous waves occupy a time synchronous with ventricular activity. Another point which may help us to differentiate the development of auricular fibrillation is the fact that the presystolic murmur which has been present usually disappears and is

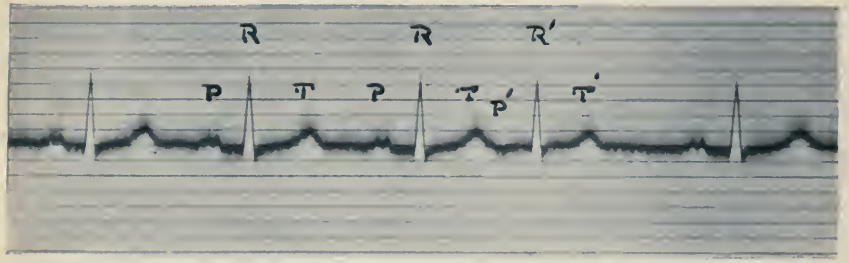

Fig. 197.—June 7, 1910. Auricular extrasystole (P′ R′ T) with compensatory pause. Note notch in P (auricular wave), indicating a defect in the auricular muscle.

replaced by a diastolic murmur terminating a short time before the first sound. That this is not, however, always a constant feature is illustrated by the present patient, who with fibrillating auricles still retains a definite crescendo presystolic murmur terminating abruptly in the first sound.

As you know, the most accurate way of obtaining information in regard to the arhythmias of the heart is by means of the electrocardiogram, and I therefore wish to direct your attention to the records of this patient.

His first record (Fig. 197) was taken in June, 1910. You will notice that for the most part the rhythm was perfectly regular, but at one point an extrasystole appears which is a contraction

occurring a little too early and is followed by the so-called compensatory pause. You will notice that the ventricular portion of the extrasystolic complex is identical in form with those of the rhythmic contractions, but that the interval between the wave which precedes this complex and the extrasystole is so short that the P wave (auricular complex) is superimposed upon the preceding T wave. This is an auricular extrasystole, which is to say that a point in the auricular wall has become overirritable and initiates this contraction. There is one other point of interest in this record to which I wish to call your attention, and that is, that the P wave of all the complexes is slightly notched. This is a deviation from the normal and indicates that the impulse is

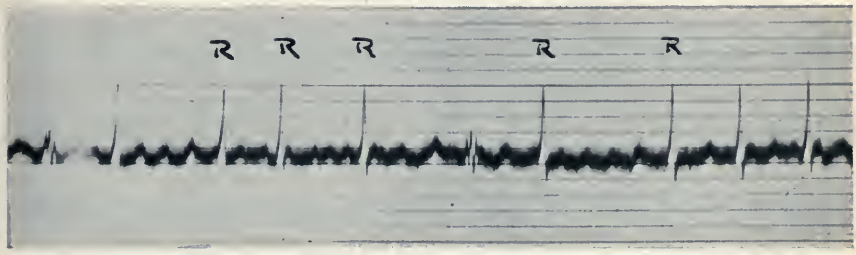

Fig. 198.—April 28, 1911. Auricular fibrillation. Rapid and very irregular. Note absence of P waves and presence of small irregular oscillations due to the fibrillating auricles. At this time the patient showed signs of cardiac insufficiency.

passing over the auricle by an abnormal path; in other words, it shows us that the auricular muscle is already slightly damaged.

The next record (Fig. 198) was taken in April, 1911. This, you will recall, was several months after his attack of pneumonia, during which he began to have complete irregularity. It was at this time that he was showing signs of cardiac insufficiency. As you will recognize, the record is one typical of auricular fibrillation. The rate is rapid, there is complete irregularity, the P wave is absent, and throughout the whole record appear small undulations characteristic of a fibrillating auricle.

Figure 199 is a portion of his electrocardiagram which was taken in April, 1915. At this time the heart was much slower

and compensation was well established. You will notice that is much slower, the rate being 68 per minute. This condition was brought about by an improvement in the heart muscle, an important element in the heart control being the continuous administration of digitalis.

The next point to which I wish to call your attention is the value of the pulse deficit as a clinical guide to our dosage of digitalis. In cases of auricular fibrillation with a rapid rate and a very irregular heart action frequently the number of the impulses which can be counted in the radial pulse is far below the actual number of cardiac contractions. Only those waves which are of considerable volume and force can be felt at the wrist, and

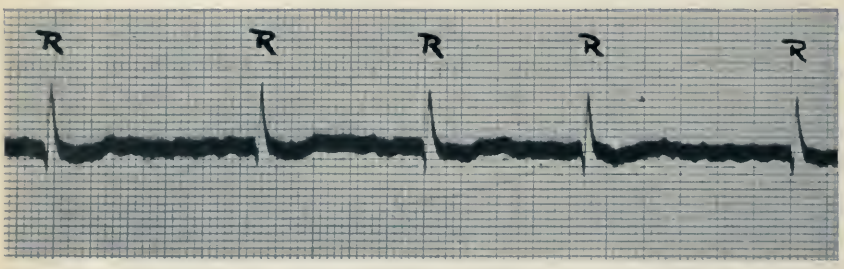

Fig. 199.—April 9, 1915. Auricular fibrillation under suitable dosage of digitalis. Heart action slow and efficient.

all the evidence of auricular fibrillation persists, but that the heart many small ventricular contractions expend their force before reaching the radial artery, and may even fail to open the aortic valves. These small contractions are ineffectual in maintaining an adequate circulation, yet are exhausting to the heart muscle, for we know that in accordance with the law discovered by Bowditch, every contraction of the heart muscle is maximal, that is to say, if it contracts at all it exhausts all of the energy stored as contractile material in its muscle-fibers at any particular moment, hence it is evident that however small the contraction may be, it must be taken into consideration in estimating the gravity of the condition of any particular heart. The inadequacy of the observations on the radial pulse alone is well illustrated in Fig. 201.

Here the lower margin of the shaded area indicates the radial count. If one were guided by this alone one would have said that on admission the cardiac rate was under 100 and usually about 70. The upper boundary of the shaded area is the count taken by auscultation at the apex, and represents much more accurately the true condition, the admission rate being 130, the gradual reduction to the neighborhood of 60 making the improvement apparent. The term "pulse deficit" is used to designate the difference in the count when taken at the apex by auscultation and at the radial pulse by palpation. Under rest and digitalis the general circulatory conditions usually improve progressively, the heart rate slows, and the pulse deficit disappears or

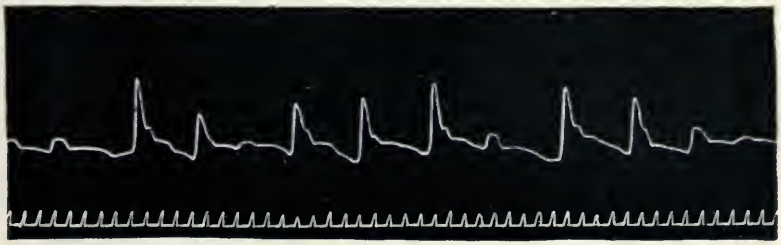

Fig. 200.—Radial pulse tracing.

becomes insignificant. I am sure that in following your cases you will find it of great advantage to keep a graphic chart of this kind, as it is an important aid in indicating the progress of the case and of regulating the digitalis administration.

Another point to which I wish to direct your attention is the question of blood-pressure in auricular fibrillation. Figure 201 is a tracing of the radial pulse of our patient at the time that he was showing cardiac insufficiency. Merely a glance at this record is sufficient to indicate to you that each individual pulse wave has a different pressure value. The blood-pressure obtained by the ordinary methods gives a very inaccurate idea of the actual condition. A much more accurate method is to determine the "average systolic blood-pressure" by the "fractional method," which is secured in the following way:

The apex and radial are counted for one minute, then a blood-pressure cuff is applied to the arm, and the pressure raised until the radial pulse is completely obliterated; the pressure is then lowered 10 mm. and held at this point for one minute, while the radial pulse is counted; the pressure is again lowered 10 mm. and a second radial count is made; this count is repeated at intervals of 10 mm. lowered pressure until the cuff-pressure is insufficient to cut off any of the radial waves (between each estimation the pressure on the arm should be lowered to 0). From the figures thus obtained the average systolic blood-pressure is calculated by multiplying the number of radial beats by the pressure under which they came through, adding together these products and dividing their sum by the number of apex-beats per minute, the resulting figure is what we have called the "average systolic blood-pressure." The following two observations made on this patient will indicate the method of computation:

April 29, 1910: Apex, 131; radial, 101; deficit, 30.

Brachial pressure.	Radial count.	
100 mm.	0	
90 mm.	13	13 x 90 = 1170
80 mm.	47 − 13 = 34	x 80 = 2720
70 mm.	75 − 47 = 28	x 70 = 1960
60 mm.	82 − 75 = 7	x 60 = 420
50 mm.	101 − 82 = 19	x 50 = 950
	Apex = 131)	7220

Average systolic blood-pressure, 55+

May 11, 1910: Apex, 79; radial, 72; deficit, 7.

Brachial pressure.	Radial count.	
120 mm.	0	
110 mm.	44	44 x 110 = 4840
100 mm.	64 − 44 = 20	x 100 = 2000
90 mm.	72 − 64 = 8	x 90 = 720
	Apex = 79)	7560

Average systolic blood-pressure, 95+

The blood-pressure determinations made in this way are of practical value in grouping our cases and in following their progress. In general, I may point out that fibrillating auricles occur mainly in two pathologic conditions: (1) cases of mitral

stenosis following the acute infections, and (2) cases of general arteriosclerosis often without valvular defects. The patients be-

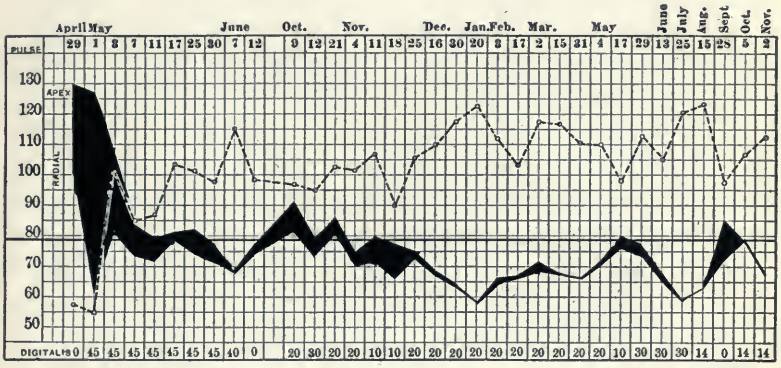

Fig. 201.—The shaded area represents the pulse deficit; the upper edge is the apex rate; the lower edge the radial rate. The unbroken line is the "average systolic blood-pressure." The figures in the digitalis column indicate minims of the tincture per day. Patient not confined to bed except for first fourteen days.

longing to Class I show a very low average systolic blood-pressure during the stage of cardiac insufficiency (Figs. 201 and 202); as

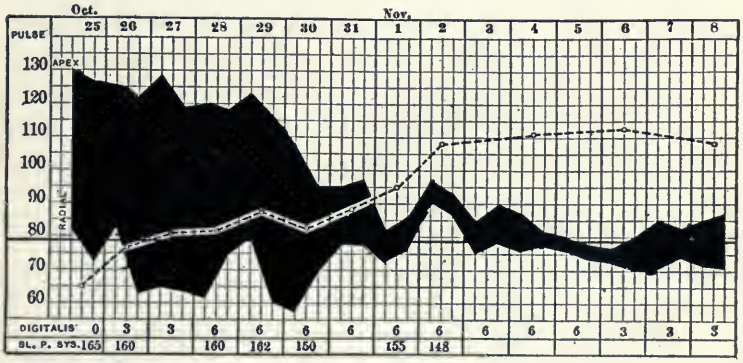

Fig. 202.—Another case, showing pulse deficit, and increase in "average systolic blood-pressure" under rest and digitalis. The lower figures indicate blood-pressure estimations taken in ordinary way; these are very misleading.

the force of the heart improves the pressure gradually rises, this is a good prognostic sign. The patients belonging to Class II

show a blood-pressure nearer the normal, and with improvement the pressure usually increases, and ultimately they show a condition of hypertension.

The treatment of this patient may be summed up in two words —rest and digitalis. As long as the patient shows cardiac insufficiency, a rapid heart, or any considerable pulse deficit, he should be kept in bed, and this should be continued long enough after the heart has become slow to allow an opportunity for hypertrophy, which progresses most satisfactorily when the diastolic rest of the heart is reasonably prolonged. This is because the blood-supply of the heart is best during the diastolic period, and if this period is too short the heart muscle does not receive an adequate supply of nutriment.

Digitalis is almost a specific in these cases. As you know, digitalis has the property of depressing conductivity. In the type of cases which we are considering the pathologic process in the heart muscle is of such a nature that it renders it particularly susceptible to the action of digitalis. Experimental investigations have shown that the depression of conductivity produced by digitalis is accomplished in two ways: first, by stimulation of the vagus, and second, by a direct action on the muscle-fiber of the heart. The effect of the administration of digitalis is to make the passage of stimuli from the auricles to the ventricles through the bundle of His more difficult. As digitalis becomes effective, more and more of the haphazard rapid and irregular impulses from the auricles are blocked. As a consequence the ventricles receive fewer stimuli and become slower and contract at more uniform intervals. They never, however, become perfectly rhythmic in their contractions.

What preparation of digitalis shall we select to obtain the most satisfactory results? I think it makes very little difference as long as you use a preparation which is active and with which you are familiar. I wish to emphasize the fact that it is most important for you to keep thoroughly familiar with the preparation which you use, you will then know whether you are giving doses which are adequate to produce the results for which you are looking. For administration by mouth I know of nothing

better than a good tincture which has been properly standardized and which is known to be active. I never use digitalis subcutaneously. I have yet to find a preparation of digitalis which is active which does not produce a very painful reaction at the point of injection. If digitalis is indicated, as is sometimes the case, in massive doses rapidly administered, the only satisfactory way to do is to use it intravenously. For this purpose digipuratum and digifolin are excellent preparations. This method should never be employed if a patient has been previously taking digitalis, since it is then impossible to estimate how much of the drug the individual will tolerate. In cases with rapid heart, a considerable pulse deficit, low blood-pressure, dyspnea, edema, and other signs of cardiac insufficiency one may begin by giving of the tincture 60 to 90 minims in the first twenty-four hours, or digifolin intravenously, 1 c.c. every six hours. After the first twenty-four hours the effect of the administration should be carefully watched, and as the heart responds the amount of the drug should be gradually diminished.

The rule for giving digitalis in these cases is to give it until you get the physiologic effect. The heart must be brought under the effect of digitalis and must be kept digitalized. The best results are obtained when one keeps the heart rate between 60 and 70, with no deficit. It is usually necessary for these patients to continue digitalis throughout their lifetime. There are occasional cases who improve to the point where they can get along without the drug, but these are very few and far between. I want to urge you most emphatically to give digitalis in these cases continuously. I see more errors committed through the giving up of digitalis in these cases than by using too much of it.

Recapitulation.—This patient illustrates:

(1) That for many years a marked valvular defect may cause no cardiac insufficiency.

(2) The early evidence of auricular myocardial change, viz., auricular extrasystoles and changes in the auricular complex of the electrocardiagram.

(3) The transition to auricular fibrillation under the stress of a new infection.

(4) The development of cardiac insufficiency when the haphazard impulses from the auricles produced a rapid, irregular, and ineffectual activity of the ventricles, with marked pulse deficit and a low blood-pressure.

(5) The general circulatory improvement associated with slowing of the heart, loss of pulse deficit, and increase in the blood-pressure under rest and digitalis.

(6) The maintainence of a fairly satisfactory circulation for many years by moderately restricting his physical and emotional activities and by the judicious and continuous use of digitalis.

CASE II.—In contrast to the first patient whom I presented to you this afternoon, I will ask you to examine with me this young woman, thirty-five years of age, single, and a stenographer. She first came to the hospital on September 19, 1917, complaining of weakness, exhaustion, digestive disturbance, and shortness of breath. As a child she had measles, whooping-cough, and diphtheria. After this she was perfectly well until at the age of twenty-four she had a severe attack of acute rheumatic fever of which the outstanding feature was a multiple arthritis of considerable severity with fever which confined her to bed for a period of six weeks. She tells me that a murmur was discovered in her heart three years after her attack of rheumatism, that is, seven years ago. She, however, noticed no subjective discomfort from this until four years ago, when she began to be short of breath on climbing stairs and developed a cough accompanied by expectoration of mucus streaked with blood. Soon after this she began to suffer from digestive disturbances. These consisted of pain in the epigastrium after eating, nausea, the formation of a great deal of gas, and from time to time attacks of vomiting.

One night in May, 1917, she suddenly was conscious of severe palpitation of the heart. This symptom had never been present before, but has continued ever since. The day following the onset of the palpitation she had a very severe gastro-intestinal upset, with vomiting and retching. She was at that time working in South America, and went to a hospital there and stayed there for three months, gradually improving

until she was able to walk about and felt reasonably well. She then came home, but was very seasick during the voyage, and on reaching New York was very short of breath and unable to walk more than a few steps. Some weeks after this she was admitted to the Presbyterian Hospital. At that time she was dyspneic and orthopneic. The veins of the neck were full and showed a marked systolic pulsation. The lungs showed dulness and many fine, moist râles at both bases. The heart was enlarged both to the right and to the left. In the apical region could be felt a presystolic thrill, with diastolic and systolic murmurs loudly heard. The pulmonic second sound was loud and accentuated. The heart was completely irregular, apex rate 156, radial 88, deficit 68. The liver could be felt in the right midclavicular line 3 cm. below the costal margin. The spleen was easily felt and was quite tender. There was no edema of the extremities. The diagnosis was made of chronic cardiac valvular disease of rheumatic origin, mitral stenosis and insufficiency, cardiac dilatation, auricular fibrillation, cardiac insufficiency. She was kept absolutely at rest and was given 45 minims of tincture of digitalis a day. Six days after admission the apex-rate was 80, radial 60, deficit 20, and she was feeling much more comfortable. She was discharged considerably improved on October 18th (apex-rate 64, radial 60, deficit 4), with instructions to limit her activities and to continue her digitalis, 10 minims of the tincture twice a day. However, she thought this was unnecessary and discontinued its use, and in spite of making very little physical effort, her heart again soon became insufficient and she returned to the hospital on October 30th in much the same condition in which she had been admitted in the middle of September. From that time up to the present she has spent at least two-thirds of her time in the hospital, improving while she is at absolute rest, but soon breaking down when she attempts to live at home.

This woman presents a very different picture from that exhibited by our first case. Instead of walking, she comes here on a stretcher. She is not, however, lying down flat, but is propped up in a sitting posture, since it is impossible for her to

breathe with comfort when her head is lower than at present. Even reclining quietly she is evidently dyspneic. Her face is worn and shows her evident anxiety. The skin and mucous membranes are pale. There is no cyanosis. The examination of the lungs shows dulness and many fine, moist râles at both bases. Over the lower portion of the back there is some subcutaneous edema which pits on pressure. The liver percusses from the fourth space and its edge is felt 5 cm. below the costal margin and is pulsating. The spleen is easily felt and is quite tender. There is no free fluid in the abdominal cavity. The legs show slight pretibial edema. I have outlined the borders of the heart as they are made out by percussion with a heavy black mark. You will observe that these are enlarged, extending in the sixth space to the anterior axillary line on the left and 5 cm. to the right of the midsternal line in the second and third spaces. There is, however, no bulging of the precordial region, but a considerable outward heave of the chest with each contraction of the heart. On palpation one can feel the pressure produced by the cardiac thrust, and in the region of the apex there is felt a fine thrill which is diastolic in time. On auscultation there is heard at the apex a long, harsh diastolic murmur, a loud broad first sound, a systolic murmur, and a sharp second sound. At the base the pulmonic second sound is accentuated and greater than the aortic second in intensity.

On account of the exquisite tenderness in the apical region I will not ask you to make a complete examination of the heart, but I want a number of you to feel the radial pulse, to observe the pulsations of the veins of the neck, and to listen to the heart in the precordial region near the base where you can study the rhythm without discomfort to the patient. On examining the pulse you will notice that it is very slow and in almost perfect rhythm at a rate of 42 per minute. The volume is fairly good, there is no evidence of arterial thickening. On listening to the heart one finds, first of all, that the rate is 84 per minute, exactly twice the rate as determined in the radial pulse. The heart sounds also show a very striking rhythm. There is a strong beat followed shortly by a weaker beat, which is, in turn,

followed by a long pause, again a strong beat, an early weak beat, and a long pause. If, while you are listening to the heart, you observe the veins of the neck, you will notice that they are quite full and pulsating clearly. There is a pulsation in the veins corresponding and synchronous with each heart-beat and the rhythm is identical with that of the heart, viz., a large wave, an early small wave followed by a long pause. There is no evidence in the veins of the neck of a presystolic wave which should be present under normal circumstances. This rhythm which you have observed is known as the "coupled rhythm."

As this sort of examination is exciting to the patient, we will now let her return to the ward and will discuss some features of her condition as you have seen them after she has left us. She presents a typical picture of mitral stenosis and insufficiency with cardiac dilatation and marked evidences of cardiac insufficiency. This, of course, has followed her severe attack of rheumatic fever, and it is clear from her history that auricular fibrillation suddenly commenced in May, 1917.

When this patient was first seen she was put on digitalis and responded to its use in a very satisfactory manner.

The heart became slow, the pulse deficit disappeared, the general circulation greatly improved, and she was able to leave the hospital in fair condition. Her electrocardiagram (Fig. 203) taken at this time shows a considerable control of the heart rate.

Since that time, however, on each occasion that she has been in the hospital it has been more and more difficult to improve the functional efficiency of the heart. The difficulty arises from the fact that the myocardial lesion has been progressive and the contractile power of the ventricular muscle has progressively diminished with an evident loss of muscle tone. Hand in hand with these changes there has appeared an increased susceptibility to digitalis, until at the present time it is almost impossible to administer doses which effectually control the heart rate without eliciting toxic symptoms.

We know experimentally that the fundamental properties

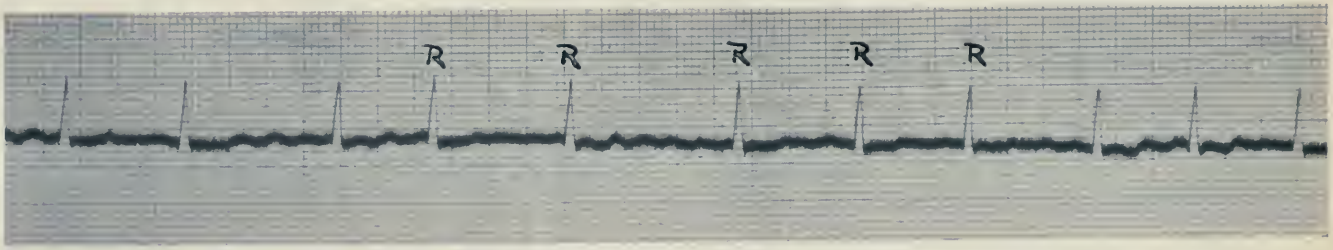

Fig. 203.—Auricular fibrillation effectively controlled by digitalis.

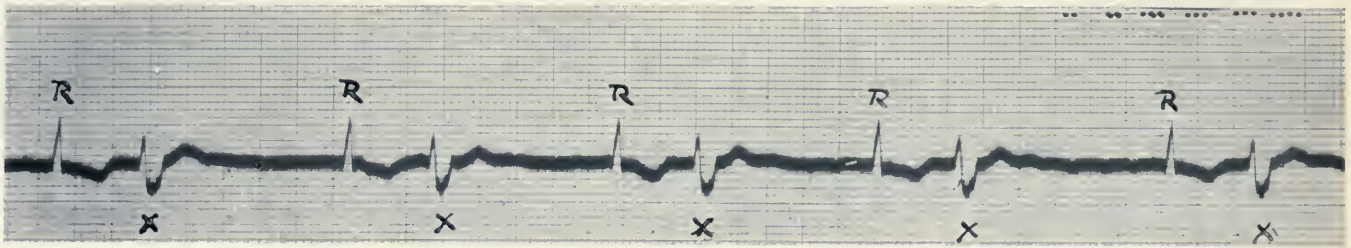

Fig. 204.—Auricular fibrillation, too much digitalis. Complete heart-block and ventricular extrasystoles producing the "coupled rhythm."

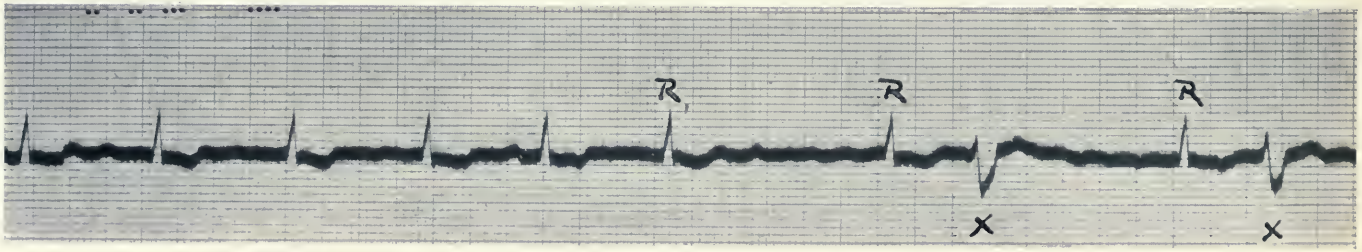

Fig. 205.—Auricular fibrillation, showing transition to "coupled rhythm."

of the heart muscle are modified by digitalis in the following particulars: (1) the conduction is depressed; (2) the muscle-fibers become more irritable; (3) the muscle tone is increased. With these facts in mind, let us examine the electrocardiagram (Fig. 204) which shows the condition which you have found on examination this afternoon. First fix your attention on the waves designated by the letter R. These conform in contour to the waves of Fig. 203, and are the normal ventricular contractions and occur rhythmically at a rate of 42 per minute. This means that digitalis has cut off all of the impulses coming from the auricles, and that the ventricles are contracting spontaneously and rhythmically quite independent of any auricular activity. In fact, we are dealing with a condition of complete heart-block. The contractions of this series are strong and effective, and are those which produce the radial pulse waves which you counted at 42 per minute. Next look at the complexes designated by X. These are of ventricular contractions which have their origin not in the bundle of His, but in a point near the apex in the ventricular wall, hence these contractions are initiated in an abnormal point and sweep over the muscle-fibers by an abnormal path, recording themselves in the electrocardiagram in these bizarre complexes. These you recognize as ventricular extrasystoles. They are due to an abnormal irritability of the muscle caused by digitalis. One would expect that the ventricle contracting in such a manner would expel its contents less effectually than when the contraction proceeded in the orderly manner originally designed by nature; such is the case as you have already observed, for while you are able to count these contractions by auscultation of the heart, and thus estimated the heart rate at 84, not one of the extrasystoles could be detected in the radial artery, hence the rate there was found to be 42. As to the question of tone, we have no accurate method of measuring this fundamental property of heart muscle, but clinically it is quite evident that diastolic relaxation is much greater than that which furnishes an effective cardiac activity.

I want you to fix this "coupled rhythm" in your mind as an important danger signal. It indicates that the patient is

getting too much digitalis. When this patient first came under observation fifteen months ago she received 45 minims of the tincture of digitalis a day and continued 30 minims a day for months with great benefit. Recently she has been taking only 15 minims a day, but even this was stopped at once when the "coupled rhythm" was discovered this morning. Figure 205 is an interesting record, as it was secured at the time of transition from her "good" rhythm to a period of "coupling." We can at once counteract part of the digitalis effect and probably abolish the coupling by the subcutaneous administration of atropin, $\frac{1}{75}$ grain, which will show its maximum effect within half an hour. This, however, will be at the expense of accelerating the heart to a rate of 100 or over. At times when a heart like this becomes oversusceptible to digitalis we can often improve matters by giving one of the bromids in combination with digitalis, and thus retain the slowing affect and at the same time do way with its irritant properties.

There is another condition which this patient presents and to which I wish to direct your attention, viz., her gastro-intestinal disturbances—the nausea, vomiting, and the formation of gas. This afternoon the symptoms were undoubtedly in part at least due to too much digitalis, but similar symptoms were present before she ever received digitalis. At those times these symptoms were due to the insufficient circulation and the consequent chronic passive congestion of her digestive apparatus. I have shown you her large pulsating liver and her large tender spleen; undoubtedly all the organs of her digestive tract are participating in this engorgement. In her earlier stay in the hospital these symptoms soon disappeared with the circulatory improvement under digitalis. The point I wish to make is that nausea and vomiting are not always due to the digitalis which is being administered, as many people, physicians included, seem to think, but if digitalis is persevered in it will in most instances correct the circulatory condition and thus cause the disappearance of the symptoms. The outlook for this young woman is not at all promising. We have been able to patch her up by regulating the heart activity on a number of occasions, but each time it

has become more difficult, and now digitalis, which she needs, fails us, since even very small doses produce toxic symptoms. It is quite possible that she may live for some months,[1] but I see no prospect of being able to improve her condition so that she will be able to leave her bed.

Recapitulation.—1. Rheumatic fever.

2. Mitral stenosis and insufficiency.

3. Auricular fibrillation, onset ten years after rheumatism.

4. Followed by a marked degree of cardiac insufficiency.

5. Gastro-intestinal disturbances due to chronic passive congestion.

6. Digitalis at first beneficial.

7. Later causing complete heart-block and ventricular irritability, as evidenced by the coupled rhythm.

COMPARISONS OF THESE CASES

I have presented to you this afternoon two cases, both have mitral stenosis following acute infections, both have auricular fibrillation. One is doing well and the outlook for him is still favorable after eight years of continuous irregularity, the other is rapidly losing ground after only fifteen months of fibrillation. Why is the heart fairly efficient in the one case and totally inefficient in the other? I think we can find the answer in the quality of the ventricular muscle which these patients present. It is quite remarkable how extraordinarily well a patient may get along with fibrillating auricles provided the integrity of the ventricles is unimpaired. In the condition of fibrillation there is no co-ordinated contraction of the auricles. They act as reservoirs for the blood entering the heart much as a dilated vein might function, the only emptying force being the elasticity of their walls. If, as is usually possible, we can with digitalis effectively cut off the auricular haphazard impulses so that the ventricles are not too greatly disturbed these will go on doing their work quite efficiently. When, however, the ventricular myocardium is correspondingly damaged, the story is quite a

[1] This patient died in the hospital in March, 1919, two months after her presentation in the clinic.

different one. Compare the ventricular condition of our two cases. In the first there is very little evidence of ventricular damage, the muscle is not overirritable, blocking is not easily produced, there are no extrasystoles of ventricular origin, the muscle tone is good, and there is comparatively little dilatation. In the second case the muscle is so excitable that a complete block and multiple ventricular extrasystoles are produced by very small doses of digitalis, and loss of tone with great dilatation is an outstanding feature.

If you study your cases carefully you will find many minor features which will aid you in predicting what the future holds in store for these patients, but the most important questions will be, How much damage has been done to the *ventricles?* and What are their capabilities for performing their work?

CLINIC OF DR. ALBERT R. LAMB

PRESBYTERIAN HOSPITAL

NON-HEMOLYTIC STREPTOCOCCUS ENDOCARDITIS

Diagnosis. Importance of Every Detail in Making a Correct Diagnosis. Course. Management. Treatment. Subsequent Results. Discussion of the Various Forms of Endocarditis.

IT is most important, gentlemen, that you should become familiar with the interesting group of cases of which today's patient is a striking representative. I emphasize this because I have found that each succeeding class is most hopelessly confused on this whole important subject, when its fundamentals are most simple. And today we shall endeavor to confine ourselves to fundamentals, leaving many of the finer points and disputed problems to the future. And this I take to be important because many of you are only too eager to discuss some still unsettled point in connection with a given disease before you have even the beginning of a clear-cut conception of the disease itself. Now, an enquiring mind, a doubting mind, an investigating mind is a priceless gift. If you have such a thing in your possession hold on to it and cultivate it. If you have not such a mind, try to develop one. The point I am making at the present time is that it is absolutely essential for each one of you to build first a foundation of complete understanding of the fundamentals for each disease or group of diseases. With such a foundation as a starting-point you may then go ahead and enquire, doubt, read, investigate, and perhaps add something to existing knowledge. But, as I have said, at the present clinic we shall stick to foundations, and if we can build a proper one for this group of diseases the afternoon will not be wasted.

Case History.—The patient, a young married woman of twenty-five, first presented herself for an opinion as to the advisability of having her tonsils removed on account of her previous attacks of rheumatism. One year before she had been feeling so exceptionally well and strong that she undertook a large number of courses in music. At the end of three months she felt weak and was obliged to drop some of her work, but did not stop entirely until another three months had passed, when, in addition to the weakness, she developed soreness in the small joints of her hands and in her finger-tips. One month later, or five months before admission, she had a severe attack of pain in the left upper quadrant of her abdomen. This persisted off and on for about a month, but has not troubled her since.

Four months ago she went to the country and felt better, but did not gain in strength as much as she had expected.

Three months ago she noticed, from time to time, a peculiar soreness in the tips of various fingers and toes. This soreness would last for a few days and then completely disappear. She says that it felt exactly as if she had gotten a thorn in her finger. During this time she noticed that her color was not so good, although she had always been pale.

For the past two months she thinks that she has had fever at times, but no temperatures have been taken. There has been a gradual loss of weight and for several weeks real night-sweats. From time to time she has had transient joint pains and more or less palpitation, with no other signs of cardiac decompensation.

Her family history is unimportant. Her habits are good. She lives in New York in the winter studying music and spends the summers on a farm. Has always been very careful about eating, drinking, exercise, and sleep. She has been married five years, but has had no children on account of her heart.

She has had measles, whooping-cough, and chicken-pox, but never scarlet fever or diphtheria. Has never been subject to sore throat, but has always had more or less nasal catarrh, with blood frequently present in the secretions. Tonsils were partially removed at eight.

At ten years of age she had her appendix removed. Shortly

after this she was kicked in the forehead and trampled on by a horse, resulting in a dislocated shoulder, "water on the knee," and dislocated fingers. Had acute otitis media with paracentesis of the drum at nineteen.

For the past seven years she has had more or less indigestion and gas associated with constipation.

At the age of twelve the patient had her first attack of rheumatic fever. She had pain in all of her joints and muscles and was confined to bed. The pain disappeared promptly, but the fever continued for two or three months. Her doctor told the family at this time that her heart was affected. The following year she had a mild attack of rheumatic fever lasting for three weeks. Seven years ago there was a third severe attack lasting for three months. Since then there has been no recurrence.

Such, gentlemen, was the story when this young woman presented herself to see if it were advisable to have her tonsils removed. She had been told by a good laryngologist that her tonsils were diseased and that they should come out if her general condition did not contraindicate it. Now I trust that it is entirely superfluous for me to utter a warning against anyone of you giving advice on such a serious question without the most careful consideration of all the facts in the case. In the first place, we must estimate the degree of cardiac damage and reach a decision as to whether the heart is well compensated and able to stand the operation. In the second place, we are face to face with the problem of why this patient has been failing in health for the past nine months with certain symptoms which we shall take up presently. Is this due to chronic infection from the tonsils or is it something else? In other words, we must not jump to the point of giving advice until we have a very clear-cut idea of the diagnosis and the patient's condition. There are no short-cuts in medicine. If you learn nothing else today, please carry away a fixed determination to go into each case completely and carefully, letting no fact escape you.

Therefore in this case we shall allow the question of tonsillectomy to wait upon the diagnosis and prognosis, and we shall find that it then answers itself.

Now, we have this patient's history up to the time of her admission to the hospital one week ago, and it has always seemed well to me to pause in any case after a history has been obtained and consider for a time what the possibilities are. For we are all too prone to take a history and make a physical examination in a routine way, and then find to our surprise that the diagnosis is still in the dark. The history suggests or should suggest certain possibilities, and by keeping these in mind during our physical examination we are much more apt to observe things which we might otherwise overlook. I know of nothing more humiliating than to have a really skilled observer go over a case and point out things which we have failed to see. You have all doubtless experienced this. But, fortunately, clever observation is largely a question of training and many things are seen because they are looked for. Now, without going into any lengthy discussion, let us see what the possibilities are in this case, then let us see how the physical examination alters these possibilities or adds new ones, and we shall find ourselves in a position to attempt a proper correlation of the known facts. Will anyone suggest a possible explanation of the patient's symptoms?

STUDENT: Pulmonary tuberculosis.

DR. LAMB: Yes, this must be kept in mind. The patient has been gradually failing in weight and strength, she has had definite night-sweats, and thinks she has had fever at times. I have asked her about cough, but she denies having had one. Many of these cases do have some cough, probably from slight cardiac decompensation, so that you may easily understand the frequency with which this disease is mistaken for pulmonary tuberculosis. If there be a pulmonary embolus with consequent hemoptysis, the mistake is even easier. What other diagnosis would you suggest?

STUDENT: Articular rheumatism.

DR. LAMB: Gentlemen, I wish that today, once and for all, you would give up the term "articular rheumatism." The proper term is "rheumatic fever." And it is much more important here than in most diseases which have been incorrectly named, for it serves to focus the attention constantly upon the joints, and

makes one forget that rheumatic fever is just as much a disease of the endocardium, myocardium, and pericardium as it is of the articulations, and that there may be associated with it tonsillitis, cutaneous lesions, chorea, pleurisy, and muscular involvement. Now, just what do you mean by saying that this may be a case of rheumatic fever? Certainly, it is not the usual picture of that disease. The patient who has had three definite attacks of rheumatic fever will tell you that she is not suffering from a similar disease at the present time.

STUDENT: I meant rheumatic endocarditis.

DR. LAMB: Now we are becoming definite. And let us always strive to be definite in medicine where we can, for, goodness knows, there is enough that is indefinite. Don't speak loosely of a case as a "myocardial affair," or as "some renal condition." Say definitely what you mean in terms of the pathologic picture. This is good training and will keep you from making many ridiculous mistakes. Rheumatic endocarditis is a most important consideration in this case. We know that she has had rheumatic fever in the past with cardiac damage, and much of her story can be explained by assuming that she has been suffering from recurring endocardial infection with whatever it is that causes rheumatic fever. We shall go into it more at length presently. Are there any other suggestions?

STUDENT: Chronic sepsis from some focal infection.

DR. LAMB: Such a condition must certainly be considered, and in going over the case we must investigate all possible sites for such infection most carefully. And, in particular, we must remember that she once had ear trouble, that there has been a chronic nasal catarrh, and that she comes to us on account of her tonsils. Most of the cases of rheumatic fever have tonsillitis or sore throat, and as this usually precedes the attack it is not surprising that most medical men consider the tonsils as the main portal of entry for the virus of rheumatic fever. While most suggestive, please bear in mind that this is not yet proved. Nor do we know whether with chronic tonsillitis there is a chronic rheumatic fever. We do know, however, that one may have an arthritis from such a source caused by streptococci,

which we believe to be a thing distinct from rheumatic fever and which should be called by its proper name, "streptococcus arthritis." We also know that in some cases of true rheumatic fever, streptococci may be isolated from the blood and affected joints. There are those, as you know, who are convinced that in these organisms we have the definite cause of rheumatic fever. We do not consider the evidence as convincing and prefer to look at these streptococci, occurring in only a small number of the rheumatic cases, as secondary invaders. Our viewpoint is, that, on the one hand, we have our cases of true rheumatic fever, and, on the other, our cases of true streptococcus arthritis, with many borderline cases whose position it is as yet impossible to establish. There is another important disease which no one has mentioned.

STUDENT: Malignant endocarditis.

DR. LAMB: Just what do you mean by that?

STUDENT: Streptococcus viridans (infection of the heart valves).

DR. LAMB: Here again we are using terms incorrectly, and as a considerable part of the difficulty in this whole subject is one of terms, I must keep insisting upon your using the correct ones. Almost any infection of the heart valves with bacteria may be a malignant endocarditis. Infection with the Streptococcus viridans, so called, is only one variety, but a most important one. And in this case it must be considered most carefully.

Now we have seen what some of the possibilities are in this case. Perhaps, in addition, we should consider some grave form of anemia or a simple, mildly incompetent heart, but neither one of these diagnoses explains the possible fever, night-sweats, pain in the left upper quadrant, transient joint pains, and sore fingers and toes. One other thing I consider of importance in any case, and that is, to remember that it may, after all, be one of unusual character; in other words, we may be dealing with a disease which we do not suspect. By remembering this in every case we are always on the lookout for something which does not fit into our explanation of the case and which may serve as a clue in directing us along the right path.

It has always seemed to me best to approach any case in the

above manner. Now this does not mean that we necessarily sit down after taking the history and go into all these details. They suggest themselves as we go along, provided that we are trained in the right way of thinking, and by the time we approach the physical examination we have, or should have, in our mind an orderly idea of the possibilities of the case. But you will need really to sit down and think over each case in this way for some time to come in order to train yourselves properly. And I believe that if you do this you will be well repaid.

And so as we finish this patient's history the case appeals to us somewhat as follows: There were in the past several attacks of rheumatic fever which caused cardiac damage. Now there is nothing to prevent a person with a damaged heart from having some entirely independent disease. But such a history is, nevertheless, important, and we shall do well never to neglect it. It is the background of the case which we must keep in mind as we go along. With such a background, this patient has been gradually failing in health for the past nine months. The symptoms of weakness, loss of weight, probable fever, night-sweats, and pallor are what we might expect from some low-grade infection. This infection might be in the nature of one of the things which we have briefly considered. But the pain in the left upper quadrant of the abdomen and the sore fingers and toes are things of the greatest importance, and should go a long way toward making a correct diagnosis if we know how to interpret them properly. It is, therefore, time to turn to an examination of the patient to see what confirmatory or contradictory evidence this examination may throw upon the case.

Physical Examination.—I think that you will at once be struck by the fact that this patient looks sick. Her eyes have the peculiar heavy appearance of one who is not well and there is an unmistakable waxy pallor. She is not dull or apathetic. On the contrary, there is a very noticeable alertness amounting almost to apprehension, such as one sees in certain types of disease. She is fairly well nourished, and the loss of weight which she has mentioned is certainly not very striking. There is no dyspnea or cyanosis. The nose, ears, sinuses, antra, and teeth show no

evidence of any foci of infection. This has been checked up by good men, and we have their assurance that these common sites for focal infection can be eliminated in this case. There are no rashes, jaundice, or eruption of any kind. The pupils are regular in outline, equal, and react promptly to light and accommodation. The tongue is moist and clean. Her tonsils are really quite small, but are adherent and somewhat cryptic, but it is not possible to express anything from these crypts. The superficial lymph-glands are not enlarged. Her thyroid is just barely visible and palpable. As you know, this is not at all uncommon in young women. There are no signs to indicate hyperthyroidism. As we have considered pulmonary tuberculosis as one of the possibilities, a very careful examination of the lungs is indicated. This has been made by several examiners and all report the lungs perfectly clear throughout. The cardiac apex is in the fifth space, 8.5 cm. to the left, and the left limit of cardiac dulness is 10 cm. to the left in the same space. No enlargement is made out to the right. The first sound at the apex is very loud, sharp, and valvular in quality. It is followed immediately by a loud, high-pitched, blowing systolic murmur heard best just within the apex, but very audible over the whole precordium. The second sound is sharply accentuated. At the base the first sound in the aortic area is partly obscured by a blowing murmur, followed by a soft second sound. The action is perfectly regular.

The abdomen shows nothing abnormal except a firm smooth spleen which descends fully 3 cm. below the costal margin on inspiration. The patient says that it was in this region that she had the pain previously described as in the left upper quadrant.

There is no edema and all of her reflexes are quite normal. The joints all appear normal at the present time. As you will notice, the tip of the right ring-finger is quite tender. It is purplish blue in color and is quite cold to the touch. Her temperature is 102.8° F., pulse 100, and respirations 24. Blood-pressure, 112/68. As the patient can give us no more information at this time we will excuse her.

We are now in a position to consider all the facts in the case available up to the present time. No matter what your

method of procedure has been up to this point, it is now up to you, before proceeding further, to argue out your tentative diagnosis or diagnoses. This should always be done in every case at the completion of your first examination. The headings "Conclusions" should be just as intrinsic a part of your case records as should the "History" and "Physical Examination." Under this heading you should state your impressions of the case with a logical analysis leading to your diagnosis. In addition, you should state your proposed line of procedure to clinch the diagnosis, your idea of the prognosis, and the line of treatment to be instituted. Where you find it impossible to decide between two or more diagnoses, I cannot too strongly recommend that you place figures of percentage of probability after each diagnosis. It is, indeed, most instructive and often most startling to look over these preliminary conclusions after a case is fully developed. The facts are there as you saw them and there is no possible way of crawling out of them. I know of nothing that is of greater assistance in developing your medical ability and in training your mind in the habit of clear and logical thinking.

In this connection let me urge each one of you to keep a card labelled "Mistakes" in your file. I trust that you will all have enough such cases to keep you duly humble, but not humiliated. Of one thing I am sure. If you will follow the advice just given you will cut down the number of your mistakes most appreciably.

Now I know that there are additional examinations which you would like to have made, but it is absolutely necessary to arrive at some tentative conclusion in regard to the case before you can know *what* examinations you require. And right here I should like to decry the way in which many of us plunge into the laboratory for aid. Many doctors feel that they cannot even consider a diagnosis until every conceivable laboratory examination has been carried out. In a recent examination at the school a case was given for discussion and diagnosis. One of the questions in connection with the case was "What additional data do you consider necessary?" I wish that you might have seen the lists of laboratory examinations requested. The striking thing was that invaraibly the worst diagnoses and discussions were from

those demanding the largest number of additional laboratory examinations. Of course, in a hospital one may have all manner of laboratory examinations carried out. But that is no reason for doing so. The laboratories are overworked, and we should all aid in making them the more effective by cutting down all unnecessary work. In private practice most people cannot afford innumerable laboratory examinations. But to my mind, even more important than either one of these considerations is the very pernicious resultant deterioration in our powers of observation and logical medical reasoning from relying on the laboratory to make our diagnoses for us. Let us ask for only such laboratory work as is distinctly indicated, let us ask for it in its order of relative importance, let us be chagrined rather than pleased if the laboratory turns up some unexpected diagnosis, and let us not cover up our inability to arrive at a diagnosis by asking for some piece of laboratory work as if it were *the* fundamental point in the case. Naturally, I do not here refer to the very obscure cases where sooner or later we have to call into play every resource of the hospital, nor to the special cases which are being worked up from the standpoint of scientific research. In general work the laboratory should be used to establish or refute the conclusions arrived at clinically, and should not be used as a substitute for a little gray matter and analysis on our part.

But let us return to our immediate task. Let us see if the examination has, in the first place, helped to rule out any of the possibilities which we considered. It is best to approach the problem from this standpoint, for it narrows it and allows us to concentrate upon a few things. Unless some new fact develops as we go on with the case, it seems to me that we are fairly safe in ruling out pulmonary tuberculosis. The lungs are quite clear and there are several facts in the case which are not explained by it.

In the same way we may be permitted to side track the diagnosis of chronic sepsis from focal infection, for we have been able to discover no such focus, and this inability has been confirmed by *x*-rays which I have not previously mentioned. Now, of course, it is not positively ruled out, and we may have to keep it

in the back of our minds until we see if the case cannot be completely cleared up on some other grounds.

We now know that this patient has fever. It is, therefore, almost certain that we have to do with something more than a mildly incompetent heart. The blood count is really part of any physical examination. In this case it was as follows: R. B. C., 4,200,000; Hg., 70 per cent.; W. B. C., 11,200; polymorphonuclears, 79 per cent.; lymphocytes, 21 per cent. We have, therefore, no grave form of anemia to deal with. It is simply a moderate secondary anemia, which, however, is belied by the patient's appearance, and a slight leukocytosis, all of which would fit in with our idea of a low-grade infection. I would remind you, however, that occasionally there is real difficulty in the differential diagnosis between this disease and pernicious anemia. While not of importance in the differential diagnosis in this particular case, you must remember that the gradual onset with fever and a palpable spleen quite commonly attracts the diagnosis of typhoid fever. In fact, these cases are most often mistaken for either typhoid or tuberculosis.

Thus our problem seems to have narrowed down to the constantly recurring one of heart, rheumatism, and bacterial infection of the heart valves, always remembering and being on the lookout for something quite unexpected. If this problem is clear in your minds you form a great exception to all recent classes.

The first fundamental point is the distinction between endocarditis and chronic cardiac valvular disease. The former is an active process which is going on in the endocardium, usually of the heart valves. Now it may be going on acutely or subacutely or chronically. The point is that it is going on. The latter is an end-result, a mechanical defect. There is no active process going on. Originally, this mechanical defect may have been caused by rheumatic fever, syphilis, or possibly some bacterial infection from which recovery took place. At the time it was taking place we had a rheumatic or syphilitic or bacterial endocarditis. When these infections ceased we passed to the mechanical results of these previously active infections and had a chronic cardiac valvular disease. When known it is well to indicate the

original cause of this. Thus we can speak of a chronic cardiac valvular disease of rheumatic origin or of bacterial origin. Arteriosclerosis, congenital anomalies, or trauma may also be the cause of mechanical defects. In our case of today we know that she had a rheumatic endocarditis at the age of twelve with probable recurrences at thirteen and eighteen. If we had seen her a year ago when she was well and strong we would have had little hesitation in saying that she had a chronic cardiac valvular disease. There was then no question of an endocarditis. Today she still has her chronic cardiac valvular disease. She will always have it. The question is whether, in addition, she now has an active process going on in the heart valves, an endocarditis, and if so, what its nature is. Now, it is not at all easy to decide in a given case whether we are dealing with the one condition or the other. But stating a problem clearly goes part way toward solving it, and if you begin to approach your cases in this manner you will gradually develop your criteria of distinction. It is, of course, quite impossible to state at what exact moment an endocarditis ceases to be one and becomes a simple mechanical defect. We all know how the mitral valve, affected by rheumatism, becomes gradually more and more stenotic, and it is an open question whether this is all simply scarring or as to whether there is not a constant slight rheumatic infection going on all the time. We cannot distinguish between the two conditions as finely as this. Where we have a valve defect without symptoms which we can recognize we are safe in calling the condition a simple chronic cardiac valvular disease. It is quite similar to the problem of deciding when an active tuberculous focus in the lung becomes a healed lesion.

The second point of great importance is for you to divest yourselves of the various terms which you do not understand and which are responsible for much of your confusion. It is just as essential that you do this here as in the case of nephritis. There is this difference, however. In the latter case there is no etiologic classification yet possible. With our present problem there is, and this is the ideal method of nomenclature. You have all heard these various terms. They include malignant

endocarditis, infectious endocarditis, ulcerative endocarditis, septic endocarditis, endocarditis lenta, subacute bacterial endocarditis, etc. As you will notice, some of these terms try to picture the pathologic picture, others attempt to indicate the prognosis, while still others approach an etiologic basis. Let us sweep them all overboard for the present and see what the facts really are. The valves of any heart may become the site of infection by practically any of the micro-organisms. In almost all instances such an infection is engrafted upon a previously damaged valve, that is, upon a chronic cardiac valvular disease. And we thus have an endocarditis. It may be acute, lasting only for days, or subacute, lasting for weeks, or chronic, in the sense of lasting for months. These terms indicating the course are really not essential, but it *is* essential to introduce the name of the infecting organism. Thus we may have a pneumococcus endocarditis, a Staphylococcus aureus endocarditis, a streptococcus endocarditis, in fact, any kind of endocarditis. And so we have the ideal etiologic terminology. Any one of these is malignant, infectious, and septic in the sense in which these terms are used. Some may be ulcerative, but this is a pathologic picture. Most are not. The terms "endocarditis lenta" and "subacute bacterial endocarditis" have been reserved for the cases due to the so-called Streptococcus viridans. But there is no more reason for continuing these terms than there would be in inventing new descriptive ones for some of the other bacterial endocarditides. The point is that we have very definite names according to the micro-organisms involved, and that keeps the whole thing straight. It is only necessary to remember and to be able to place these various other names in order that we may understand what some people are talking about when they use them.

Now, naturally, the various endocarditides vary more or less according to the causative organism. Some of the forms are well understood; others much less so. Today it is not our purpose to go into these differential features, interesting though they be. If you can only get a proper framework for the whole subject now it will be comparatively simple for you to add to the structure as you go along. As you meet each new type, you can

study it, read about it, and perhaps do some real investigation upon it. It will all fit into your general scheme in an orderly manner.

About one type you know or should know a great deal, namely, syphilitic endocarditis. According to our scheme this is a Spirochæta pallida endocarditis, but there is absolutely no harm in using the other term, as it means the same thing. This form, more particularly the aortitis part of it, is so well known now that it is generally considered apart from the bacterial endocarditides, although it belongs there just as truly as do any of the others.

Another well-recognized form and one which directly concerns us today is the rheumatic endocarditis. It, too, is almost always separately considered, although, without doubt, it belongs in this general group in spite of the fact that the causative agent is probably still unknown. The term "rheumatic" is used in place of the micro-organism just as the term "syphilitic" is used in place of Spirochæta pallida. It has a well-recognized pathology, and as it is, by all odds, the most common cause of endocarditis it is of the greatest importance. We could easily spend several afternoons on rheumatic fever and its various manifestations, but for the present we must content ourselves with a consideration of some of the important points concerning rheumatic endocarditis. Clinically, there is no way of deciding definitely whether a case is one of rheumatic endocarditis or not. That is, there is no decisive test, such as a complement-fixation reaction or the isolation of the causative agent by blood-culture. But in most cases this form of endocarditis is associated with a definite attack of rheumatic fever with all of its characteristic features. None of us should fail to recognize such a case. In the second place, we frequently see cases where the joint symptoms rapidly clear up, but where the endocarditis progresses. These cases are not always recognized. You will do well to think a bit about them. If a patient has recovered from the acute symptoms of rheumatic fever, but still runs a slight temperature, has a pulse elevated out of proportion to this temperature, and develops a heart murmur, changes the quality of an

existing murmur or develops an additional one, I think that you are justified in considering that that patient has rheumatic endocarditis.

Obviously, our patient does not fit into either of the above groups. Our troubles begin when we reach the third and most tantalizing group, that in which there is a true rheumatic endocarditis with only the most transient or fleeting joint symptoms or with none at all. No one knows how large this group is. We do know, however, that it exists, and I suspect that it is much more important than most of us realize. You have all, I am sure, been impressed by the fact that the cardiac damage does not run in proportion to the severity of the attack of rheumatic fever. You have seen most extensive damage from the mildest cases, and the reverse. Some of you have seen a case recently in the wards. This boy entered the hospital with a considerable fever and high pulse. It was quite unexplained until the second day, when he developed a transient pericarditis. This disappeared the same day, but his temperature did not return to normal, and in the course of a short time he developed heart murmurs and was ill for some time. He had never had rheumatism and at no time during his course did he have any joint symptoms. Repeated blood-cultures were negative. Now, as I have said, we have no means at our disposal to settle this question, but in the absence of any positive evidence pointing to any other type of infection I feel that we are justified in considering this a case of rheumatic endocarditis and pericarditis. And please remember in this connection that although we are emphasizing the endocarditis, in practically every case of rheumatic infection all parts of the heart are affected. Sufficient importance has not been attached to these cases. Otherwise we would not hear so much about cases of idiopathic mitral stenosis. A very large number of such cases must be examples of rheumatic endocarditis which went unrecognized because of the absence of joint symptoms. This is a fruitful field for investigation, but the question will probably not be settled until the cause of rheumatism is surely discovered.

The only other group of endocarditis which interests us today

is probably the best known of them all, and yet it was only a few years ago that many consultants made or enhanced their reputations by its diagnosis. I believe that each and every one of you should be able to recognize it by the time you leave school. As a matter of fact, I fear that there is more danger of your making the diagnosis when the disease does not exist than there is in your missing it when it does. It is by no means rare, and you will have the opportunity of seeing several cases before you graduate. I refer to the so-called Streptococcus viridans endocarditis. This is not the right name for these streptococci, for they do not all produce green on blood-agar-plates, as the name viridans would indicate. Also, you should not use the term "Streptococcus mitior," introduced by Schottmüller as descriptive of the organism's low virulence, as other streptococci may be of low virulence. They are, however, all non-hemolytic, and this term is, therefore, the correct one. The disease has very definite characteristics which distinguish it from the various other varieties of bacterial endocarditis, except that due to the influenza bacillus. These two forms are indistinguishable clinically. Influenza endocarditis is quite rare. Nephritis is supposed to be a frequent complication. But the distinction is made between the two only by blood-culture. They differ from all the other forms in being strikingly subacute or chronic. One should have no more difficulty in diagnosing non-hemolytic streptococcus endocarditis than one should have in recognizing a well-marked case of typhoid fever. We shall take up its characteristics as we proceed with the analysis of our case.

The way is now clear for us to round up our case. The first thing necessary in arriving at any diagnosis is correct observation. That is, if we have left out important points in the history or examination the whole thing is as hopeless as a picture puzzle from which many pieces are missing. So to start with, let us assume that we have skipped nothing of real importance. In the second place, the symptoms and signs point more or less clearly to one or more conditions. And in this regard we have narrowed our problem down to a differential diagnosis between rheumatic and some other form of bacterial endocarditis, probably non-

hemolytic streptococcus. And this is a constantly recurring problem, and it is here that you will make your mistakes in diagnosing non-hemolytic endocarditis when it does not exist. Your problem in these cases is this: You have a case of chronic cardiac valvular disease who is well and running a temperature. The first thing to do is to be sure that this patient has not some disease entirely unassociated with the heart valves. As I have previously said, there is nothing to prevent such a person having typhoid fever or malaria or anything else. With such possibilities out of the way the second thing to do is to consider whether you are dealing with the fever so often seen with a badly compensated heart. If there is no decompensation this possibility automatically disappears. If there is decompensation we know that it is possible for the patient to run a temperature until compensation is re-established. I do not think we know what this fever is due to. In some cases it is from small patches of bronchopneumonia, or infarcts, or infections which are analogous to terminal infections. The decision here between fever with decompensation and some form of bacterial endocarditis is not easy. But observation and blood-cultures usually suffice to settle the question. At any rate, it does not concern us with our present patient. If we can thus rule out the above conditions, we come to rheumatic versus some form of bacterial endocarditis, and the former can be decided upon only by elimination and by the things in the history and examination which do not fit.

And these things which do not fit form the third important step in diagnosis. In any case a certain number of the symptoms and signs are completely explained by our tentative diagnosis. There are usually, however, one or more things which are not explained. They do not fit into the picture. And I am in the habit of asking you to ring these misfits and to consider them most carefully, for in a great many cases it is the proper appraisal of these facts which do not fit that spells success or failure in solving the problem. We always like to explain all the facts upon the basis of one disease if possible. Sometimes it is undoubtedly wise not to do so, but I am positive of one thing, and that is that you will make a serious mistake if you carelessly

introduce some new disease or complication to fit each unexplained fact.

Now with our case, most of the facts can be explained by rheumatic endocarditis, but there are some which cannot. The pain in the left upper quadrant is one misfit. You might explain it as a pleurisy, which is not infrequent in rheumatism, but we have investigated it more closely and find that it was too low for a pleural pain. As a matter of fact, it was over the spleen, which we find very distinctly enlarged. There is nothing in her past history to account for an enlarged spleen, and it is certainly not the spleen of chronic passive congestion, for she has not this condition. We shall not go far wrong in interpreting this symptom and sign as due to an infarct. Now an infarct from rheumatic endocarditis practically does not occur. If the heart is decompensated there may be a thrombus in one of the auricles or even in one of the ventricles with a resultant embolus, but this is a result of the decompensation and not of the rheumatic endocarditis. Embolism is no part of rheumatic endocarditis. On the other hand, it is exceedingly common in non-hemolytic streptococcus endocarditis. As our patient is not decompensated we have gone a long way toward ruling out rheumatic endocarditis by this one misfit.

The tender toes and fingers, with the appearance which you have seen in one of them, are no part of rheumatic endocarditis and are classical for the other conditions, so that I feel that in conjunction with the above we can dismiss rheumatic endocarditis.

Therefore, by the process of exclusion we have arrived at the diagnosis of non-hemolytic streptococcus endocarditis, or of some condition of which we have not even thought. Now let us see if the facts all fit the former, or if we have some things still unexplained.

Practically every case of this disease is engrafted upon a preexisting chronic cardiac valvular disease, usually of rheumatic origin. This is an essential background for the diagnosis. And so we start right, for our patient has had such a condition for a number of years. And here I must interject a warning: Always

remember that a patient with a valvular defect is a potential candidate for a non-hemolytic streptococcus endocarditis. It must always enter into your prognosis of any case of chronic cardiac valvular disease, though you do not need to terrify the patient with your idea, and you must always remember its possibility when such a patient is failing in health. If you will always bear this in mind you will not be apt to miss any case, for, as the late Dr. E. G. Janeway was accustomed to say, whenever a rare disease turned up unexpectedly, "I believe we could make that diagnosis if we could only remember at the time we saw it that such a disease existed."

The onset of the disease is as insidious as the disease itself. The patient has simply not been feeling as well as usual since "before Christmas" or since "last fall." Probably most of these patients have been suffering from the disease for weeks before they even realize that they are not well. Our patient had been failing since some time about nine months before. She had tender fingers six months ago and her splenic infarct five months ago. As both of these symptoms are characteristic of the disease, we can feel almost certain that she was well in its clutches some six months before she felt it necessary to consult a physician, and then not because she considered herself seriously ill, but simply to find out if she would not be better off without her tonsils.

From the time these cases are first seen they have fever. It is very slight at first, often not more than half a degree or a degree in the afternoon. Some afternoons it may not be elevated at all. Such a low-grade fever may go on for several weeks before it begins rather wider swings. As the disease progresses there may be four or five degrees between the high and the low. We have no temperature records for our patient, but she has volunteered the information that she thinks she had fever at times, and for the past week it has run between 99° and 101° F.

Loss of weight and strength are constantly present and progressive, as in our case. They do not loose rapidly, but they do it persistently.

There is a slowly developing anemia. Like the rest of the

disease, it is insidiously progressive. In the terminal stages it is usually most extreme. It is practically uninfluenced by iron and arsenic, but for a time is remarkably benefited by transfusions. Our case is not so anemic according to her blood count as we have a right to expect. As a matter of fact, I think that you will agree with me that her appearance belies her count, and that we may, therefore, doubt its accuracy. We shall have it repeated.

None of these patients shows a normal color. Many have a very characteristic café-au-lait color, which is most suggestive. But this is not essential. The others have an appearance much like that you have just seen. It is a waxy, almost transparent pallor, either quite white or with a dirty tinge bordering on the café-au-lait.

Night-sweats are quite common at almost any time in the course, as are chilly sensations. Real chills are usually seen only in the later stages.

It is not at all unusual to have mild, fleeting joint pains, as in this case, and also pain, soreness, and stiffness in various muscles, but the joint pains do not approach in severity those of rheumatic fever.

Thus far the symptoms are not characteristic. They are simply what one would expect with many a low-grade infection, and from them one cannot make a diagnosis. The important point is that they occur upon the background of a chronic cardiac valvular disease. This should make us extremely suspicious, and, being suspicious, we can look more closely for symptoms and signs which are bordering upon the pathognomonic. It is often a fact that the symptoms which are of the highest significance are not volunteered by the patient. They may not have attracted attention because of their trivial nature or they may have been forgotten. Thus in our case the sore fingers and toes were not mentioned until the question was definitely asked, as the patient had interpreted them as part of what she considered rheumatic manifestations.

And yet these sore fingers and toes are among the highly characteristic symptoms of the disease. They occur at some

time in the course of most of the cases. They come on suddenly, are quite painful, feel numb or prickly and cold, have the purplish-blue color with whiteness of the rest of the tip, as you have seen, and clear up in the course of a few days. It is not usual to find them in any other condition, so that if they are definitely present in conjunction with such other symptoms, as we have found in this case, they should go a long way toward determining the diagnosis.

The pain in the splenic region with the presence of an easily palpable, hard spleen is another thing of great significance. Like the sore fingers, this comes on quite suddenly, but it is apt to last for a considerable length of time. The pain is sharp and stabbing in character and is generally made worse by inspiration. As you know, this is due to an embolus, as are the sore fingers and toes. One frequently has to ask for this symptom, as the patient may well skip it or simply remark that she had some pain in her stomach. So you see that it is absolutely necessary for you to know that these facts are among the fundamentals in the diagnosis of this group of diseases. If the patient has had pain in "the stomach" it is up to you to locate it exactly, and if it be in the splenic region and be corroborated by a palpable spleen you have facts which are essential in the diagnosis.

Now a splenic infarct does not necessarily mean non-hemolytic streptococcus endocarditis or any other form of endocarditis. They are fairly common, as you will note if you watch for them. They mean that somewhere in the body there is a thrombus located so that it is possible for an embolus to reach the spleen. This source is usually the left side of the heart. It may be from vegetations on the valves or from a thrombus in one of the chambers. Now, as you are aware, it is most extremely unusual to have a thrombus in either the auricle or ventricle, except where there is a considerable degree of decompensation or in the rare cases of coronary thrombosis. If there is real decompensation and an infarct occurs one should hesitate a long time before ascribing it to the form of endocarditis which we are considering. It would help not at all in the diagnosis, which would have to be made by other means. We need scarcely go

into the cases of coronary thrombosis. If such decompensation be not present and we have an infarct we may well think seriously of an endocarditis, of course, remembering other possible sources for thrombi. One thing we know is that rheumatic endocarditis *per se* does not cause embolic phenomena, or at best such an occurrence must be so rare as to justify us in practically precluding it. Most of the other forms of bacterial endocarditis do cause emboli, and especially the one which we are discussing. So that the occurrence of emboli is an important differential point in the diagnosis between rheumatic and non-hemolytic streptococcus endocarditis.

And what has been said about splenic infarcts and the sore fingers and toes applies equally to other embolic phenomena, such as infarction of the kidney, cerebral embolus, and embolic aneurysms. In a suspected case of bacterial endocarditis one should keep a sharp watch for emboli of any organ. The point is that those of the fingers and toes and spleen are the most common and most readily recognized. A cerebral embolus speaks for itself. Renal infarcts are quite common. In addition to the pain in the costovertebral angle which is quite commonly absent, the striking thing is the presence of red blood-cells in the urine.

We have thus far considered all the symptoms and signs which this case presents. We find that there are no misfits. That is, everything can be explained by the diagnosis which we have arrived at, and by it better than by any other. There is not a single clue pointing in any other direction, so I feel that we are safe in discarding the possibility of some quite unthought of condition.

As you will remember, further back we discussed some of the steps necessary in arriving at any diagnosis. At this point it is well to point out a fourth necessity. And that is to see if there are missing signs and symptoms which are important in the diagnosis, and if there are such things absent, are they important enough to make our conclusions impossible. Of course, none of you expects every symptom and sign of a given disease to be present in every case of that disease. But it might well happen and frequently does that enough important ones are absent to

make the diagnosis unjustifiable. As a matter of fact, some of the men on the staff who had the opportunity of observing this case would not commit themselves on account of the absence of at least one such point. Can any one suggest essential missing data?

STUDENT: Petechiæ.

DR. LAMB: That is the point. Petechiæ are most important in this disease. I doubt if there are any cases in which they do not appear at some time in the course. Their continued absence should make one very suspicious. But they must be looked for, not casually, but with the most painstaking care. Every part of the body must be examined every day, and you must remember to look in the mouth and in every part of the conjunctiva and also at the eye-grounds. Up to the present time, in spite of the most careful search, we have failed to find a single petechia. And yet, gentlemen, I feel that we have enough positive evidence to justify our diagnosis clinically, and I feel certain that petechiæ will be found. And I want to urge you to have the courage of your diagnostic convictions. If you have argued a case out carefully and arrived at a conclusion that seems justified, do not be afraid to say that that is what you think the case is. Also I want to urge you to take every opportunity to become familiar with the appearance of petechiæ. I am constantly surprised at the number of men who do not know them when they see them. I see no use in going into any description of these spots. The only way to become familiar with them is to see and study them. Most of you confuse them with telangiectases. Study these, too, for you must know the difference. Petechiæ are not limited to the form of bacterial endocarditis which we are considering. They may be present in many conditions, and it is well to remember that they may occur in the late stages of chronic cardiac valvular disease. It is not unusual to see men fooled into a diagnosis of bacterial endocarditis by their presence in such a condition, and I think that you will make more mistakes in diagnosing non-hemolytic streptococcus endocarditis simply because petechiæ are present than you will in failing to diagnose it because they are absent. If the case shapes up right

otherwise, however, they are a most important determining factor. Are there any other important points to consider?

STUDENT: How about tenderness of the sternum?

DR. LAMB: We do not find this sign in many of the cases, and it is possible to elicit it in cases other than those of this disease. Therefore, we have never rated it as an important sign. It is interesting and worth looking for, but I do not believe that it should influence us much in our decision. It has not been present in this case.

From a clinical standpoint I feel that we have now covered the essential points of the subject. And we come to the determining point in diagnosis, namely, clinching it by means of the laboratory. If you could have only one piece of laboratory work carried out, what would you request?

STUDENT: A blood-culture.

DR. LAMB: Yes, that is absolutely essential. And the second thing you would request would be another blood-culture to check the first, if it has been positive, or to endeavor to get a positive one if it has been negative. And if negative and your analysis of the case has led you to the decision which we have here reached, you should keep on taking blood-cultures until the case is settled in your mind. For as you know, one may obtain several negative cultures before having a positive one. Also remember that where you have several negative cultures in a case that still seems to be one of non-hemolytic streptococcus endocarditis you may be dealing with a case of infection by the influenza bacillus. Remembering this, you can take appropriate measures to grow this organism. Your blood-culture should be plated, as it is a more certain means of getting positive results where there are but few organisms, and it also gives one, for comparative purposes, a means of estimating the degree of bacteriemia through the count of the colonies.

A blood-culture was taken on our patient on admission, and the plates showed an average of 41 colonies per cubic centimeter of a non-hemolytic streptococcus, which in this case was a viridans. This was confirmed. Thus it seems to me that we have tracked down this case to an unescapable conclusion. We have

established the diagnosis, there is no present reason to believe that there is any complication, and I think you will agree with me that the question of tonsillectomy has been automatically settled.

Now the patient and family are not especially interested in all of our technical discussions. They want to know in simple language what the trouble is, but what they are mainly concerned about are the chances for recovery and the length of time the illness will last. This brings us to the much-neglected field of prognosis. We have not the time to go into the general principles of this question. A whole afternoon could be thus spent most profitably. In this disease you must know, in the first place, that it lasts for a long time, from many months up to two years. Therefore, you have to prepare all concerned for a long siege. Our patient has been ill for some nine months already. As two years is practically an extreme limit for its duration, we can pretty confidently predict that another six months, or slightly more at the most, will see the end. That is, we are in for a siege of several months rather than one of a few weeks. And on top of this distressing information we have to add a climax of hopelessness. It is about as insidiously fatal as any disease can be. Hemsted has reported one case of apparent recovery, and Libman, whose experience in this disease is very wide, says that he has seen 3 cases recover out of a total of over 250 which he has observed. But certainly recoveries are so rare that we must consider the disease as practically uniformly fatal. One may hold out a faint ray of hope that an exceedingly rare case has not ended fatally. All of these facts must be imparted to some responsible members of the family, but I think there is only rarely justification for taking away all hope from the patient. They are generally satisfied with the information that there is a bacterial infection of the heart valves, that the fight is to get rid of these bacteria, and that it generally takes a long time. Everyone then settles down to the long fight, and the disease is so insidiously progressive that the patient scarcely realizes the fact that he is loosing ground slowly but surely.

You must remember to remind the family of the possibility

of the various complications which are apt to occur, such as the various types of emboli, especially cerebral, eventual cardiac decompensation, progressive anemia, pneumonia, and possible tuberculosis.

In regard to the so-called bacteria-free cases or healed cases I can only refer you to Dr. Emanuel Libman's articles. It is a most interesting aspect of the disease about which he knows more than anyone else.

Treatment includes all of the measures known to build up the patient's general condition, and, in addition, there have been used various measures of serum and vaccine therapy and transfusions. As I shall hope to show you this patient again or at least tell you the outcome of the case, we shall take these up at that time.

Subsequent Course.—You will remember that early in the fall I showed you a case of non-hemolytic streptococcus endocarditis. (A brief summary of the case was here given.) This patient died during the middle of March, a little over five months after you saw her, or, as nearly as we can tell, about fourteen months after the onset. This is just about what one expects in these cases.

Shortly after you saw her petechiæ were discovered, as we predicted. Although never very abundant, some were usually present. She also had frequent tender fingers and toes and transient joint and muscle pains. There was an embolus to the tip of her right ear and rather numerous ones to her spleen and kidneys.

On January 10th there was a sudden complete left hemiplegia, from the effects of which she never completely recovered.

The temperature was irregular between 99° and 102° F., with occasional shoots to 104° F. The pulse was correspondingly elevated. There were frequent night-sweats, but chills were not a prominent feature. For some time the appetite was fair and then failed almost entirely. Loss of weight was progressive. Anemia was overcome and controlled for a long time by transfusions, but then became progressively marked.

Her heart never increased appreciably in size and she never suffered from any real decompensation. She developed numer-

ous extrasystoles and several changes in the quality of her systolic murmur, but no new murmur appeared.

On February 20th she left the hospital for her home and, without the appearance of any new complications, flickered out like a candle about one month later. It is quite striking that during this month she had no fever.

The autopsy revealed the usual typical picture of the disease. I have not time to go into it at this moment, for I wish to emphasize the treatment.

The patient was most intelligent. She never lost hope, and thus we had the best possible co-operation. Every possible supporting measure was used to keep her generally in the best condition.

For a time she had autogenous vaccines. They did absolutely no good, and were only used because the family wished it. Sensitized vaccines were not used. They do no more good than the others in this condition. We might just as well realize and accept the fact that in non-hemolytic streptococcus endocarditis vaccines, in large doses or small, at long intervals or short, sensitized or unsensitized, do absolutely no good.

Transfusions were used repeatedly. The blood was obtained from two different donors, one of whom was vaccinated with small doses of her organism, the other with large doses. As far as could be determined, there was no difference in the effect on the patient. In all she received eleven transfusions with a total of about 2600 c.c. of blood. Now, as I have said, the transfusions controlled the anemia for a long time and in this way undoubtedly prolonged her life. This we have seen repeatedly in these cases where the transfusions were not confused with vaccines. As anemia plays quite a considerable part in the downward path we may accept transfusions as an important therapeutic measure in these cases. We feel that they are valuable, but not as cures.

These transfusions from vaccinated donors were futile in sterilizing the blood-stream. This corresponds with our experience in the past and with that of others. To be sure, there was frequently a slight reduction in the number of colonies following

a transfusion, but this we see with straight transfusions and even after saline infusions. Here the number of colonies per cubic centimeter when treatment was started was 119. During its course the lowest number recorded was 63. So that in this case, as with others, all experience is against this procedure.

As this method was a failure, we tried large doses of serum from a vaccinated pony. In one week she received 700 c.c. of this serum. The colonies diminished to 41, but four days later were at the maximum for her—295. So that we accomplished nothing but a moderately severe serum sickness. In this connection it is of much interest to note what Dr. Cole of the Rockefeller Hospital has told me. He says that occasionally a horse highly immune to the pneumococcus will get up a pneumococcus endocarditis.

Our present-day methods against this disease are powerless. It is well to recognize this and to have the courage to give up repeating the same old useless procedures.

Before closing this case I want to give you a list of the more important references. It is most important for you to file them away for future reference. You must read these articles to round out your knowledge of the disease. In them you will find all the other references. If you have not yet started a proper system of medical filing, get busy at once, for you can do nothing in medical practice, research, or teaching without such a system.

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CLINICAL TALK BY DR. LEO BUERGER

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CYSTITIS: A DISCUSSION CONCERNING ITS DIAGNOSIS

Inadequacy of Prevailing Methods in Arriving at a Diagnosis of Cystitis. Importance of Cystoscopic and *x*-Ray Examinations in Correctly Interpreting the Pathologic Changes Leading to this Condition. Illustrative Cases.

ALTHOUGH it is a most laudable ambition on the part of the practitioner to attempt to diagnosticate as nearly as possible the pathologic and anatomic lesions that he believes responsible for a certain group of symptoms in any given patient, a wider and more comprehensive knowledge of certain special fields of medicine have taught the specialist that it is much better in many cases to refrain from making anything more than a tentative diagnosis, lest grave errors—mistakes that may do incalculable harm to the patient—be made.

It is true that a grouping of the *cystitides* according to etiology, the pathologic changes or lesions, or possibly the special organisms responsible may be of considerable value for purposes of enhancing our academic knowledge and even in furthering therapeutic progress. Nevertheless, it may be accepted as an axiom, that the *diagnosis of cystitis is one that the practitioner or internist neither can nor should make.*

Were the elaborate, interesting, and comprehensive chapters on cystitis in our medical text-books when prepared for the practitioner provided with an inscription "Never make the diagnosis of cystitis, but be satisfied with the observation that the patient presents the symptoms of *cystitis*," our students would assume a totally different attitude toward that large variegated group

of cases which are now indiscriminately labeled as "cystitis," presumably masquerade as cystitis, but, in reality, suffer from a multitude of other lesions.

Were this exposition to do nothing else but emphasize that an attempt to make a diagnosis of cystitis from symptomatology and from certain easily ascertainable objective findings—such as urinary findings—is not only futile but fallacious, it will have accomplished its purpose. Let us pause for a moment to recount the case of a young girl who recently consulted me, and who had been treated for many weeks by her physician as a case of acute cystitis with the usual bladder irrigations, who had been becoming progressively worse in spite of the treatment—for here we have a most illuminating example of the worthlessness of clinical signs even when coupled with laboratory examinations, in the diagnosis of so-called cystitis.

CASE I.—*Foreign Body, Encrusted (Petrified) Catheter in Contracted, Intensely Inflamed, Ulcerated Bladder of Female Giving Symptoms of Cystitis.*

A. A., female, consulted me December 30, 1918, with a story that she had been in perfect health until about three months ago, when her bladder symptoms began. Since then she has complained of great frequency of urination, intense pain during the act, the symptoms becoming daily more and more severe, so that now she must void every ten or fifteen minutes during the day, and gets up at least three or four times during the night. She had been receiving daily irrigations of the bladder for more than six weeks without noticing any improvement whatsoever.

Cystoscopy, December 30, 1919, revealed an intensely inflamed, very much contracted, irritable bladder, the site of an intense cystitis, harboring a foreign body that gave the appearance of a coiled-up bougie or catheter of about No. 18 French, almost completely encrusted with lime or phosphatic salts.

On January 10, 1919, at operative cystoscopy done under anesthesia, with the author's operating cystoscope inserted into the bladder, the encrusted catheter was easily brought into view, the grasping or punch forceps of the operating cystoscope introduced through the special telescope made to seize the catheter, and the foreign body easily removed in the well-recognized, typical fashion, allowing the cystoscope to emerge first, the catheter in the grasp of the forceps following (Fig. 206).

The clinical lesson to be drawn from cases of this sort—and such errors in diagnosis occur not infrequently—may be summed up as follows: The symptoms of cystitis are not to be depended upon in diagnosis, for they give us no true knowledge as to the real lesion responsible for the clinical manifestations, the cystitis being but one of the products or complications, as it were, of a more profound or more serious affection; and finally, that treatment based upon symptomatic diagnostic conclusions can be of

Fig. 206.—Encrusted catheter removed through operating cystoscope in case treated for cystitis.

no avail. In fact, it may be well to emphasize right here at the beginning that the symptoms of cystitis do not at any time warrant the diagnosis of this affection any more than the recognition of sequelæ or complications of any other disease will explain the nature of the original malady. It is only with the application of the cystoscope, aided at times with the *x*-ray examination, that the correct interpretation of the existing pathologic conditions is possible.

The urologist who not infrequently encounters cases with su-

pravesical lesions, when the mere clinical signs suggest the presence of a cystitis, has learned to apply the cystoscope, and no longer relies upon his examinations of urine and what the history may reveal. Not infrequently will an inflammatory lesion of the kidney with or without renal lithiasis masquerade under the guise of so-called "cystitis." The following case will illustrate:

CASE II.—*Infected Hydronephrosis, Multiple Renal Calculi, Ureteral Stricture at the Ureteropelvic Junction, Marked Perinephritis, Being the Lesions Discovered at the Time of Nephrectomy in a Patient who Consulted Me for Urinary Frequency and So-called Cystitis.*

R. S., female, May 23, 1914, gave a history of having bladder trouble, diagnosticated as inflammation. Recently she had another attack, voiding every fifteen minutes. Symptoms referable to the kidneys had been absent, except on one occasion some indefinite pain across the back.

Cystoscopy May 14, 1914, revealed evidences of cystitis, but disclosed that the chief lesion was in the right kidney. Catheterized specimens from the right kidney showed the presence of pus-cells and some red blood-cells, and markedly diminished functional capacity of that kidney.

x-Ray examination showed a calculus about $\frac{3}{4}$ inch long and $\frac{1}{2}$ inch wide, and several smaller calculi in the lower pole of the right kidney, and another stone presumably at the ureteropelvic junction measuring $1\frac{1}{8}$ inches in length by $\frac{1}{2}$ inch in width.

May 29, 1914, typical nephrectomy revealed an infected hydronephrotic kidney harboring the calculi described in the *x*-ray report, with marked dilatation both of the extra- and intrarenal pelves, an enormous hilus lipoma, marked perirenal inflammation, the calculi being situated in the pelvis and calyces.

At the ureteropelvic junction a stricture, probably of inflammatory nature, was observed, and in the cortex near the upper pole there was a small mixed tumor measuring less than $\frac{3}{4}$ inch in diameter.

Clinical Course.—Almost immediately after the removal of the offending organ there was complete cessation of the symptoms of cystitis.

Symptoms of cystitis, therefore, may be the expression either of the reflex action of a diseased kidney with calculi, or the result of bladder lesions produced by the action of infected urine secreted by a diseased kidney.

The symptoms of cystitis may be the only ones, or at least the complaint which prompts the patient to consult the physician or the surgeon, even though a most extensive inflammatory lesion of the kidney, with or without calculus, may be present, for the latter may give no symptoms until the onset of extensive suppurative renal infarction brings about fever and chills.

CASE III.—*Cystitis Symptoms Predominating in a Case of Pyelonephritis, Infected Hydronephrosis, Calculus in the Upper Ureter, Perinephritis, Stricture of the Lower Ureter Associated with Cystitis, Complicated Later by Multiple Cortical Abscesses, Suppurative Renal Infarction Requiring Nephrectomy.*

M. S., female, consulted me on the 29th of October, 1918, because of urinary frequency, urgency, nocturia (three times at night), dysuria. She had been operated upon six months previously for a uterine condition, and the uterus was said to have been removed. It was only after careful questioning that she admitted having had intermittent lumbar pain, but this was not definitely located, and did not seem to annoy her sufficiently to be worthy of note.

Cystoscopy demonstrated an inflamed bladder (cystitis). The specimens from the left kidney were negative, but an obstruction was encountered at a point 8 cm. removed from the right ureteral orifice. No urine was obtained from the right kidney, and because of the marked pyuria it seemed more than likely that the pus content of the urine was attributable to an infection of the right kidney.

x-Ray examination October 31, 1918, showed a shadow opposite the third lumbar vertebra, about $\frac{1}{2}$ inch in length, presumably at the hilus of a somewhat enlarged right renal shadow. Although these findings were not very definite, the shadow was sufficiently distinct to warrant the suspicion that a renal or pelvic stone was present.

It was decided, therefore, that it would be advisable because of the pyuria and the obstruction in the right ureter to explore the right kidney, the diagnosis of hydropyonephrosis being made in view of the large amount of pus that was present in the bladder. This advice the patient refused to follow, and she passed out of my hands until December 1, 1918, when she consulted me in great distress, having had an attack of fever and exquisite lumbar pain so severe that she said "she could stand it no longer."

The patient was referred to the hospital, and on the 8th of

December her temperature rose to 105° F., and there was a distinctly palpable mass in the right loin.

December 9th nephrectomy was done.

Pathologist's Report.—*Kidney Specimen.*—The kidney is more than twice the normal size, capsule very much thickened

Fig. 207.—Hydronephrotic kidney, showing two large foci of suppurative infarction which infiltrate the parenchyma.

and edematous, there being a considerable increase in the fatty tissue about the kidney and renal hilus. When the kidney is opened a large amount of purulent urine is evacuated. The pelvis is very much distended, and on section (Fig. 207) two large foci of suppurative infarction can be seen to infiltrate the paren-

chyma, causing a prominence at the external border of the kidney (Fig. 207), this on surface section showing numerous areas of purulent infiltration. In the capsule numerous miliary ab-

Fig. 208.—Same case as Fig. 207, depicting prominence at external border of kidney, and ureteral calculus.

scesses are seen on the surface of the organ, and at the upper pole there is another focus of suppurative infarction.

In the ureter, just within a few centimeters of the pelvis, there

is a calculus about ½ inch in length, embedded in swollen, velvety red, purplish mucous membrane, the ureteral wall being thickened to about 3 to 5 mm. in this neighborhood (Fig. 208).

Here was a woman operated upon for uterine trouble with a stricture low down in the ureter, suspected as being the result of inclusion of the ureter in a ligature, who had a shadow in the upper ureter region, near the pelvis of the kidney, hazy, it is true, but nevertheless somewhat suggestive, and who sought relief particularly because of bladder symptoms, *frequency of micturition, urgency, and pain on urination.* On palpation we found a somewhat enlarged kidney, and on cystoscopic examination an obstruction at 8 cm. in the right ureter.

Clinically interesting was this case because of the fact that *frequency of urination predominated in the picture* until the occurrence of suppurative infarction in the kidney.

Clinical Conclusions.—Cystitis, therefore, as suggested by the above striking illustrative examples may be merely a complication or concomitant resulting irritative local vesical alteration, brought about by an infection of one or more portions of the supravesical urinary tracts.

Vesical calculi, too, associated with infection of one or both kidneys or infection combined with renal lithiasis may give clinical pictures that may readily be confused with those of so-called cystitis. Just as foreign bodies of the bladder and other lesions to which we shall later refer may clinically simulate those manifestations of deranged micturition usually incorrectly set down by the practitioner as "cystitis," so also large vesical calculi may be completely overlooked unless the methods of cystoscopy and *x*-ray examination be applied.

Before occupying ourselves with a detailed discussion of some of the many pathologic lesions that may be overlooked when a diagnosis of cystitis is made on clinical symptoms alone, let us cite one very striking example of the insidious nature of renal and vesical lesions as far as localizing symptoms are concerned.

CASE IV.—*A man with the symptoms of chronic cystitis develops a most extensive infection of one kidney, with marked perinephritis,*

multiple abscesses of the kidney, without at any time presenting any manifestations of pain or lumbar tenderness in the region of the affected kidney, although bladder symptoms have been present for a long time, and some of the toxic symptoms and effects of absorption had been developed a short time before nephrectomy was carried out.

M. N., male, consulted me December 28, 1917, the history being that of *protracted cystitis*, possibly associated with stricture.

x-Ray examination revealed a vesical calculus, which on some of the plates had a spheric outline $2\frac{1}{3}$ inches in diameter, in others had an elliptical shape $2\frac{5}{8}$ x $1\frac{1}{2}$ inches in diameter.

Suprapubic cystotomy was carried out on January 10, 1918, and the calculus removed, the patient making an uneventful recovery, except for one attack just before his discharge from the hospital, which afterward was diagnosticated as a possible evidence of pyelonephritis.

The suprapubic wound healed promptly after the removal of the drainage-tubes, and the patient left the hospital with practically no disturbances of micturition, but showing the distinct signs of severe attacks of pyelonephritis. He did not appear strong and healthy, and recurrences of attacks of pyelonephritis were considered extremely likely, and, in fact, were to be expected.

The patient was again admitted to the Mt. Sinai Hospital on February 27th, with a temperature of 101° F., no renal tenderness, a haggard look, and urine containing a fairly large amount of pus. It was again a question as to whether the temperature was due to the infection of the left kidney without local manifestations, or whether some intercurrent or other infection, such as tuberculosis, was present.

On February 28, 1918, another cystoscopic examination was performed to determine whether we were dealing with retention of purulent urine in the kidney or not. At this time it was easy to obtain a perfectly good view of the bladder, because the stone had been removed, and the mucous membrane was found almost normal except for some congestion. It was with surprise that *two ureters were discovered* on the left side, the upper or posterior one doubtlessly having been covered up by the large calculus at our previous cystoscopic examination. All three ureters were catheterized, specimens being obtained from the right kidney, and from the upper or posterior and lower or anterior ureteral orifices on the left side.

	Right.	Left upper.	Left lower.
Reaction	Acid.	Acid.	Acid.
Albumin	Trace.	Trace.	Trace.
Urea	1.1 per cent.	1.4 per cent.	0.7 per cent.
Microscopic	Few epithelial cells.	Few epithelial cells.	Few epithelial cells.
	Few red blood-cells.	Few red blood-cells.	Few red blood-cells.
	No pus-cells.	No pus-cells.	Many pus-cells.
	Few hyaline casts.	Few hyaline casts.	Few hyaline casts.
Culture	Sterile.	Bacillus coli communior.	Bacillus coli communior.

To summarize, we have a fairly normal functionating right kidney with urine containing a trace of albumin; a left kidney containing two pelves, the lower pelvis corresponding to the upper ureter, presumably normal except for the presence of Bacillus coli communior in culture, and an upper pelvis evidently infected with urine containing many pus-cells, diminished urea output, and infected with Bacillus coli communior.

Thus, we were dealing with a man who had had recurrent attacks of pyelonephritis in a kidney with a double pelvis, the lower portion of which was evidently healthy, the other or upper portion harboring one or two calculi, and the seat of an extensive pyelonephritis.

Diagnostic Conclusions.—In a man who had had a large vesical calculus, and in whom the *x*-ray findings indicated the presence of a fair-sized calculus in the left kidney, the clinical course as well as the cystoscopic findings pointed to severe infection of at least the upper half of the left kidney, the lower pelvis being uninvolved. The insidious nature of the process as evidenced by the absence of local pain, renal colic, or local tenderness, the presence of attacks of fever with general symptoms rather than localizing phenomena, made the interpretation of the clinical course and the surgical indications somewhat difficult. However, from a consideration of the findings, it was possible to make the following deduction regarding the anatomic lesions present.

Thus, we surmised that the upper portion of the kidney was the seat of an inflammatory process with multiple abscesses, or at least extensive pyelonephritis, and suppurative areas in the

parenchyma; and furthermore, because of the long history, and the absence of a true pyonephrosis (as indicated by cystoscopic

Fig. 209.—Infected kidney with double pelvis. Deposition of inflamed fat about the upper two-thirds of the kidney; enlarged upper ureter; normal lower ureter; normal lower pole, with cut surface through the isthmus.

findings), and the absence of pain and tenderness, we were in all probability dealing with an inflamed kidney, whose exterior was

enveloped in markedly thickened perirenal adipose tissue, that is, a kidney surrounded by enormous fat production, and enveloped as it were or encased in a mass of inflammatory tissue. The operative findings corroborated these diagnostic inferences.

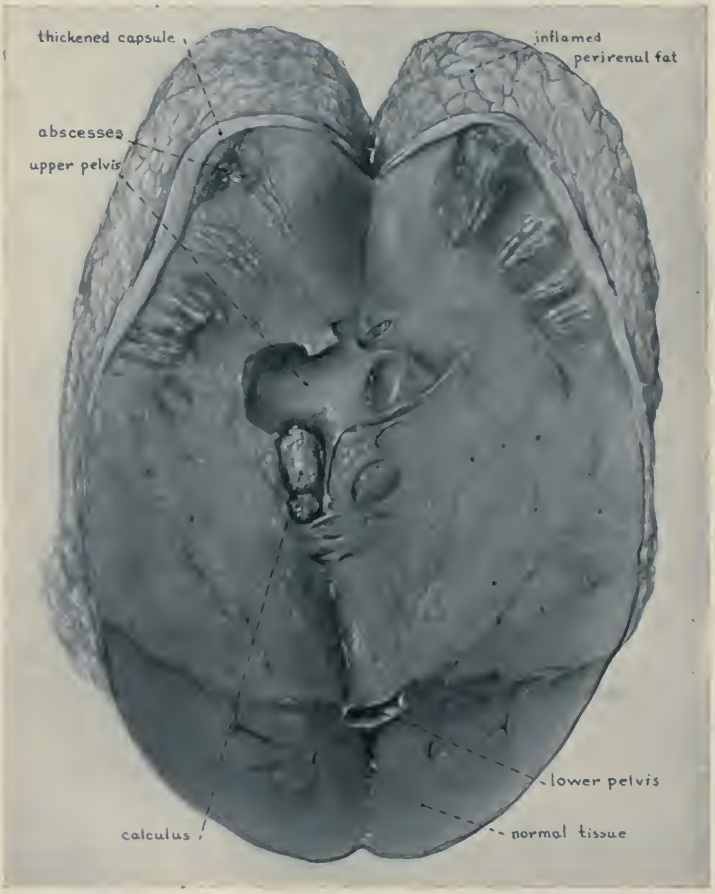

Fig. 210.—Kidney bisected, showing perirenal inflammatory fat, two stones in upper pelvis, with multiple abscesses, inflamed edematous upper three-fourths of parenchyma and normal lower pole.

Operation, March 5, 1918, typical nephrectomy through the usual Albarran incision, with the removal of an infected kidney

provided with two pelves and fused by its lower pole with the sister organ of the other side (Figs. 209, 210).

Is it permissible, then, for the practitioner to make a diagnosis of cystitis? In a general way it may be suggested that a tentative diagnosis of cystitis may be made without danger of falling into error, particularly in those cases which present acute symptoms of but short duration, one week or two at the most, and in which a complete recovery follows as far as all subjective manifestations and urinary changes is concerned. But even in such instances, as will be shown later on, further investigation of the character of the bladder interior and the condition of the kidneys and ureteral tract, supplemented by the *x*-ray is advisable, lest lesions of great import be overlooked. *In the chronic cases a purely clinical diagnosis of cystitis is in the present state of our knowledge of urology fraught with grave danger and may jeopardize the health of the patient, as well as be responsible for the destruction of a kidney that might otherwise be saved.*

Before entering into a detailed discussion of just how far our clinical judgment in the recognition of cases of so-called cystitis may be allowed to venture, let us pass in review some of the many pathologic conditions that may offer a clinical syndrome indistinguishable from the text-book picture of cystitis, and that may be grouped according to the site of the process, as follows:

Lesions With Symptoms Simulating Cystitis

RENAL LESIONS

1. Tuberculosis of the kidney (very common).
2. Calculi with or without infection.
3. Hydronephrosis.
4. Urinary concretions.
5. Renal crises with bladder symptoms.
6. Pyelitis.
7. Pyelonephritis.
8. Pyonephrosis.
9. Metastatic or embolic infectious lesions.

URETERAL LESIONS

1. Ureteral calculi.

BLADDER LESIONS

1. Tuberculosis.
2. Ulcers.
3. Foreign bodies.
4. Calculi and concretions.
5. Tumors of the bladder, carcinomata, papillomata.
6. Leukoplakia.
7. Malakoplakia.
8. Syphilis.
9. Edematous lesions about the sphincter, being an extension of lesions in the urethra and prostate.
10. Intravesical intrusion of prostatic adenomata (Albarran lobe).
11. Diverticula.

LESIONS OF THE BLADDER NECK

1. Fibrosis of the sphincteric region.
2. Contracture of the neck of the bladder (including so-called median bar).
3. Submucous adenomata and fibromata.

PROSTATIC LESIONS

1. Prostatitis.
2. Prostatic congestion.
3. So-called hypertrophy or fibro-adenoma, or adenoma.
4. Fibrosis.
5. Tuberculosis.
6. Carcinoma.
7. Prostatic abscess.
8. Rare prostatic tumors (sarcoma).
9. Prostatic calculi.

LESIONS OF THE SEMINAL VESICLES

1. Vesiculitis and perivesiculitis.
2. Tuberculosis.

URETHRAL LESIONS

1. Gonorrheal urethritis.
2. Stricture of the urethra.
3. Calculus in the posterior urethra, particularly behind the verumontanum.
4. Malformation and urethral ureter.

In addition to this large array of pathologic processes that may simulate and give symptoms of cystitis, there are causes outside of the bladder (extravesical) that may be responsible for similar manifestations. They are as follows:

EXTRAVESICAL LESIONS

1. Pelvic abscess (infection from the adnexa and uterus).
2. Pelvic abscess from appendicitis.
3. Tumors of the uterus and adnexa.
4. Hemorrhoids and carcinoma of the rectum.
5. Vesicovaginal fistulæ.
6. Vesico-intestinal fistulæ.
7. Pericystitis, etc.

In addition to these may be mentioned a number of other general conditions that may present pollakiuria and even urgency, and that are often mistaken for cystitis. Thus, may be mentioned—

1. Constipation.
2. Onanism, with congestion of the sexual organs.
3. Neuroses.
4. Chemical alterations of urine: phosphaturia, etc.

CLINICAL LESSONS IN DIFFERENTIAL DIAGNOSIS

To enumerate and recite in detail case illustrations exemplifying erroneous interpretation of conditions indicated merely by

name in the above lists would take me far beyond the scope of this lecture. Let us rather, therefore, cite only a few instances in the groups mentioned here, where symptomatology has been deceptive, and other means for diagnosis had to be employed.

Renal Tuberculosis Simulating Cystitis.—When a mother comes to you complaining of persistent bed wetting in the case of her child, although he or she has attained the age of six, eight, or ten years, and has perhaps noticed, too, that the child voids more frequently than it should—be this phenomenon unaccompanied by any other manifestations—the possibility of the existence of a tuberculous process in one kidney and in the bladder must be thoroughly entertained. *For frequency of urination is so often the initial symptom of a renal tuberculosis and mistaken for cystitis that the presence of this condition must ever be borne in mind.* So that, when a child who appears to be somewhat too old to continue to have *enuresis nocturna* comes to us for examination, a specimen of urine is to be carefully scrutinized for the presence of pus and tubercle bacilli, and we will not infrequently be surprised to find an enlarged kidney plus tubercle bacilli in the urine of a child who has been regarded as having either enuresis nocturna or cystitis.

The busy urologist is wont to see almost daily an individual whose bladder has been washed for weeks or months, whose urinary frequency, urgency, nocturia, painful micturition, and pyuria have been attributed to and treated for simple inflammation of the bladder. The stories of such patients offer a clinical lesson that is not only most illuminating in emphasizing the futility of basing diagnosis on the means at the disposal of the practitioner, but is also of sufficient importance to demonstrate the mistake of applying treatment before a positive diagnosis has been made. For it is because of the incorrect attitude of security and false hope of future cure instilled into the patient by the initiation of local methods of therapy that the patient is lulled into a mistaken feeling of confidence and anticipation of early relief from a distressing complaint which is certain to become worse as the days pass by, coupled with daily extension of tuberculous lesions in the bladder as well as in the kidneys, each

moment of procrastination decreasing the ultimate chances of permanent recovery.

Renal and Vesical Tuberculosis Without Tubercle Bacilli in the Urine.—It is because of the difficulty of finding tubercle bacilli in many cases of renal and vesical tuberculosis that even the urologist is apt to be mistaken, and may find it difficult to be certain as to the exact nature of the lesion he has to deal with. The application of the cystoscope, however, will demonstrate that one kidney is involved or suspicious of tuberculosis, and will lead the experienced urologic surgeon to make a tentative diagnosis of renal tuberculosis, even though shadows of calculi may be demonstrated in the *x*-ray, and even though these are distinctly seen within the renal shadow of a suspected kidney.

It is not only with the cystoscope that the diagnosis of renal tuberculosis can be made, but the practitioner has at his disposal a very simple method in which he should acquire experience, namely, *that of detecting the existence of a tubercular ureter by palpation through the vagina.*[1] Were a routine vaginal examination carefully made with a view to palpating a diseased ureter in all instances of suspected cystitis in married women, many errors could be avoided. *Just as the differential diagnosis between chronic appendicitis in women and a ureteral calculus low down in the ureter, lies within the reach of the examining finger, so also the induration of a tuberculous ureter will become readily recognizable after some practice.*

CASE V.—*Case Treated for Eight Months for Cystitis, with a Stone Shadow Within the Right Renal Area, an Indurated Ureter Felt per Vaginam, an Ulcerative Cystitis with Urine Negative for Tuberculosis, Proved to Have a Tuberculous Process by the Removal of a Tuberculous Kidney Harboring Stone.*

H. S., female, had been troubled with urinary frequency for about eight months, there being a burning pain during the act, bladder irrigations having been recommended by her physician for "cystitis."

Cystoscopy, March 11, 1918, revealed an intense cystitis

[1] In the male, rectal examination will often disclose data of value either in the form of tuberculous vesicles or prostate, and more rarely a thickened ureter may be felt.

with superficial purulent exudate over superficial erosions or ulcerations, an obstruction in the right ureter at 4 cm. above the right ureteral orifice, an absence of flow from the right kidney, the specimens from the left kidney being negative and showing good renal function. The bladder specimens showed pus, trace of albumin, no sugar, numerous *streptococci and bacilli in spreads, tubercle bacilli being absent.*

x-Ray examination disclosed two shadows within the right renal area, each about 1 cm. in diameter, between the second and third lumbar transverse processes, doubtlessly indicative of the presence of calculi. The renal outline was suggestive of a large organ. In the pelvic region at a point corresponding to the site of the ureteral obstruction there was a suggestive shadow, possibly a calculus or calcification in the ureter.

Vaginal examination disclosed a hard ureter, an indurated mass, which could have been mistaken for peri-ureteritis, or could have been regarded as an inflamed ureter of the tuberculous variety.

Tentative Diagnosis.—In brief, in a case with vesical symptoms, possibly right ureteral colic, with urine containing *no* tubercle bacilli, but pus, whose right ureter was obstructed at a point 4 cm. from the vesical orifice, whose left kidney was normal, and whose *x*-ray plates showed two stones in the right kidney, and a possible small stone in the right ureter, the question arose as to whether we were dealing with a case of calculous disease alone, with obliteration of the right ureter due to calculus in the ureter and consequent inflammation, or whether we were dealing with a combination of renal tuberculosis and renal calculi. Was it expedient to go down on the right ureter with the view to removing the calculus suggested by the shadow in the plate, or was it preferable to go in on the kidney which per abdomen could be palpated as distinctly enlarged, and which doubtless harbored at least two calculi?

In view of the absence of tubercle bacilli a positive diagnosis could not be made, but because of the ureteral obstruction, the uncertainty of the nature of the ureteral shadow, because of the presence of the hard cord felt per vaginam, and because of the feeling that the removal of the ureteral calculus in such a hard ureter could not be followed by good functional results, it was decided to expose the kidney, which I proceeded to do at the New York Polyclinic Hospital and Medical School March 14, 1918.

March 14, 1918, nephrectomy through an Albarran incision revealed *a very much enlarged tuberculous kidney*, and a ureter

about the thickness of a man's thumb was liberated and cut through with some difficulty. The kidney was removed in the usual fasion and the specimen revealed the following (Fig. 211).

The kidney was almost twice the normal size, surrounded by an enormous amount of perinephritic inflammatory tissue. On section it showed a distinctly tuberculous kidney, in the pelvis

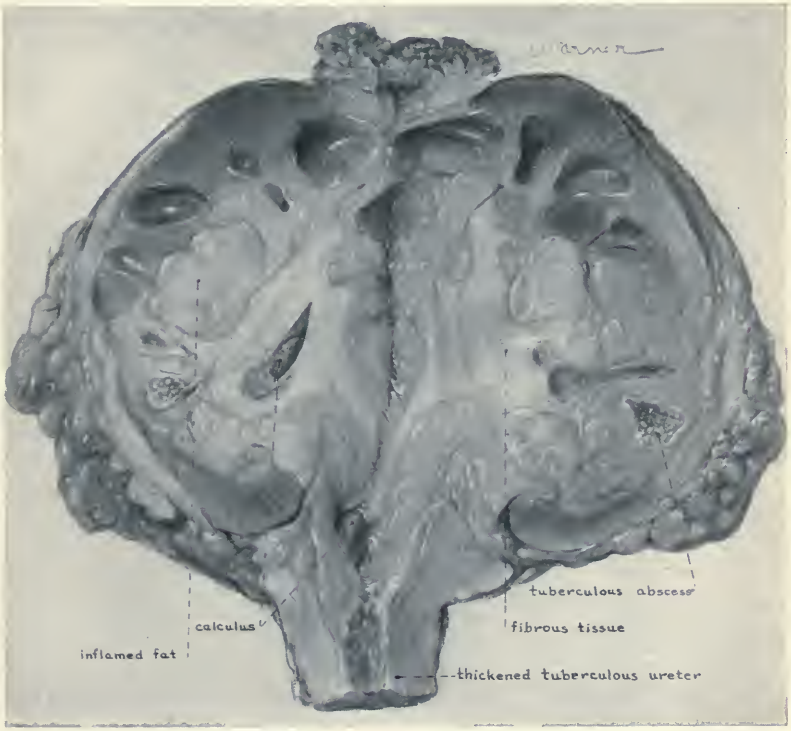

Fig. 211.—Tuberculous kidney with calculi in a case diagnosticated as cystitis.

of which two calculi were lodged. Interesting was the very large amount of fat formation in and about the pelvis and in the hilus, the dense masses of connective tissue about the pelvis, and the cavities, some of which were tuberculous and some due to the secondary dilatation produced by the presence of the calculi. The ureter showed the typical tuberculous lesions, its walls being enormously thickened (Fig. 211).

Conclusions.—We have here an illuminating example demonstrating, first, the wisdom of exposing rather the kidney than the ureter when we are in doubt regarding the presence of a tuberculous lesion, and one proving, second, that unless a shadow in the lower ureter be definite, the presence of an indurated cord per vaginam must be regarded rather as an evidence of tuberculous

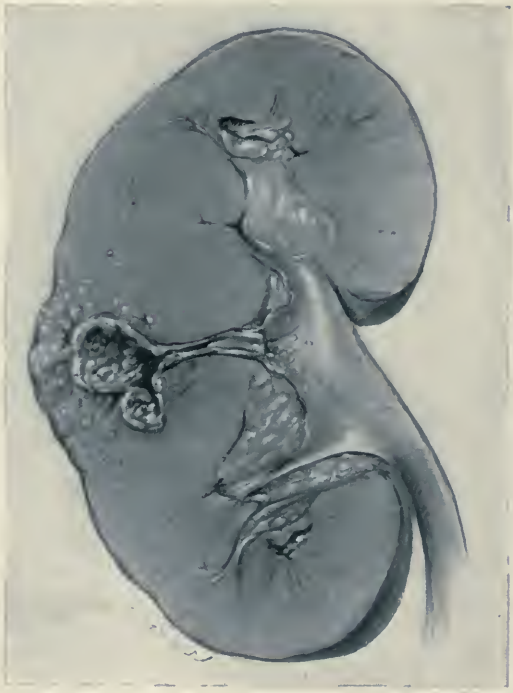

Fig. 212.—Tuberculous kidney, showing development of tuberculous cavity and miliary tubercles in a case treated for cystitis.

ureteritis than of the presence of a calculus unless the outline of such calculus be distinctly felt, and third, indicating again the *error of entertaining a diagnosis of cystitis when the true nature of the lesions can only be ascertained by special urologic methods.*

Tuberculosis of the Kidney Diagnosticated as Cystitis and Treated as Such.—Cases of this sort are so numerous in my own

records that it would be a work of supererogation to do other than merely cite a few striking examples.

CASE VI.—*Tuberculosis of the Kidney with Symptoms of Cystitis, Diagnosticated as Such and Treated as Such for Six Months; Operated Upon for Uterine Trouble, in Order to Cure the Cystitis.*

L. R., female, consulted me August 27, 1917. She had had increased frequency of urination for about six months, and had been passing urine every ten to fifteen minutes during the day, as well as at night. Three months previously she had been operated upon at a hospital in the city, with the diagnosis of cystitis, the latter having been regarded as due to pressure of her uterus. No relief of the symptoms after operation was obtained, the pain on voiding and the frequency persisting and being intense and becoming more severe.

Cystoscopic examination made the diagnosis of right renal tuberculosis a positive one.

The kidney specimen obtained by nephrectomy (Fig. 212) showed an organ almost normal in external appearance, except that over the middle of its convex border there was a large area, over whose surface there were numerous solitary and agminated tubercles. Corresponding to this on section, as well as illustrated in the figure, there was a tuberculous cavity with numerous tubercles in the neighborhood.

CASE VII.—*Renal Tuberculosis Giving the Symptoms of Cystitis Only, in a Case Treated with Bladder Irrigations for More than Six Months, the Kidney Showing Extensive Cavernous Tuberculous Lesions.*

M. U., female, had been complaining of painful and frequent urination for six months, for which she was treated with bladder irrigations, the diagnosis of cystitis having been made.

Cystoscopic examination made on May 21, 1918, made the diagnosis of left renal tuberculosis easy, the usual lesions of tuberculosis being present in the bladder, the specimens from the left kidney containing pus and tubercle bacilli.

Nephrectomy on June 1, 1918, revealed an enormous hydroureter due to stenosis of the lower end of the ureter by reason of tuberculous lesions, and the kidney seen in Fig. 213 of the typical cavernous tuberculous type containing large cavities lined with cheesy tuberculous material.

This case illustrates beautifully how extensive the lesions in the kidney may become while the patient is being treated for "cystitis."

Gonorrheal Infection of the Ureter and Kidney Pelvis Simulating Cystitis.—The fallacy of treating cases for cystitis, when

Fig. 213.—Tuberculosis of the kidney with extensive cheesy degeneration and cavity formation in case diagnosticated as cystitis.

we may be dealing with an infection of the whole urinary tract perpetuated by a focus of gonorrheal infection in the ureter or pelvis of one or both kidneys, is well illustrated by the following case, which is not at all unique in this sense.

CASE VIII.—*Gonorrheal Infection of the Bladder; Gonorrheal Ureteritis with Stricture Formation; Gonorrheal Pyelitis and Ureteritis Cured by Lavage with Argyrol, in a Case Treated for Cystitis.*

L. B., male, said that he had "an infection" (presumably gonorrhea) about one year previously. Although the usual source of infection was denied, there seemed to have been no doubt regarding the diagnosis, because he had had a severe infection of the conjunctiva that was attributed by the eye specialist to the urethral discharge. Over a period of a year he had sought the advice of numerous physicians; had received bladder irrigations almost daily for a period of more than seven months, and, on July 27, 1915, was said to have had a *very severe cystitis with considerable pus in the urine.* Latterly he gave up all treatment because of the persistence of his symptoms, the pyuria, the vesical symptoms, bladder irritability continuing, in spite of the vigorous treatment he had received during the past year.

Cystoscopic examination showed rather unusual lesions, which may possibly be characteristic of gonorrheal inflammation of the bladder. The floor of the bladder showed a considerable amount of inflammation, particularly about the left ureter, where the edema, the thickening and velvety condition of the mucosa extended somewhat over the paratrigonal regions and distally well into the sphincter. There were numerous strawberry-like papular lesions, more angry red than the follicular lesions seen so frequently in the cystitis of females, and in the posterior wall of the bladder there were numerous minute bodies, some of which seemed to be lymphoid follicles, others cystic (cystitis follicularis et cystica). The specimens obtained from the right kidney showed that indigo-carmin appeared in good concentration after a lapse of fourteen minutes, the urine being perfectly clear. From the left kidney, however, the urine was turbid. From the exploration of the left ureter it appeared that there were evidences of retention of urine here, that there was an obstruction in the lower ureter that could be overcome with manipulation; that there were evidences of ureteritis, and possibly pyelitis, the involvement of the lower ureter being indicated by the fact that more turbid urine was obtained from the lower ureter than from the upper. In short, a tentative diagnosis of gonorrheal ureteritis with a tendency to stricture formation and of gonorrheal pyelitis could be made.

Laboratory examinations did not reveal the presence of gonococci in either the spreads or cultures from the right kidney urine, but gonococci were found in culture and spreads from all

the five specimens collected from the left kidney, a fact which practically rules out contamination with the catheter. Positive findings are also reported in the specimens obtained from the bladder. The presence of pus-cells in the left specimens further corroborated the diagnosis of infection of the ureter and pelvis of the kidney with the gonococcus. An *x*-ray examination on January 8th was negative. On January 13th cystoscopy was again done, and the pelvis of the kidney and ureter were washed out with 15 c.c. of a 20 per cent. argyrol solution, about 5 c.c. being allowed to remain in the renal pelvis, the pelvis and ureter being irrigated with the rest of the solution.

In short, a case of undoubted gonorrheal infection of the left ureter and left renal pelvis and bladder wall, the patient having been given one treatment of the pelvis and ureter with 20 per cent. argyrol. The improvement was most remarkable after this treatment, so that a subsequent cystoscopy showed that the bladder was very much improved, the granular appearance having almost disappeared.

Within three weeks the patient was well.

Enough has been adduced in the way of clinical material to demonstrate how tuberculosis of the kidney *par excellence*, as well as renal calculi with or without infection, pyelitis, and pyelonephritis, may offer insufficient clinical evidence to warrant the diagnosis of a renal affection without the aid of cystoscopic and *x*-ray examination, and how bladder and so-called cystitis symptoms may dominate the clinical picture.

One other type of insidious encroachement upon the integrity of the renal organs by metastatic or embolic bacterial invasions may be worthy of brief mention.

Metastatic or Embolic Infectious Renal Lesions Without Renal Symptoms Mimicking the Clinical Picture of Cystitis

Case IX.—W. E., running the gamut of multiple suppurative lesions from an unknown primary focus after a short period of bacterial invasion of the blood with Staphylococcus aureus, suddenly voided cloudy urine, accompanied with frequency, urgency, and the usual symptoms of cystitis. There were no symptoms referable to either kidney, no tenderness, no enlargement of these organs, but the pyuria persisted.

Cystoscopy demonstrated that the specimens from the right

kidney were freely admixed with pus, which on culture exhibited Staphylococcus aureus.

Diagnosis.—Embolic infection of the right kidney with Staphylococcus aureus, the foci communicating freely with the pelvis.

Another and even more remarkable instance of the fleeting transitory course of certain types of embolic renal infections that complicate a *Staphylococcus aureus* lesion elsewhere in the body, with total absence of any symptoms referable to the kidney, was noted in one of our recent cases.

Case X.—M. E. presented an indolent infection of the dorsum of the foot, accompanied with edema of the foot, and an enlarged inguinal node, and the usual evidences of lymphangitis extending from the foot to the knee. An incision over the abscess evacuated pus which could be traced upward for some 5 inches along the lymphatic channels, all of these being widely laid open and the wound packed.

Two days later there was a chill, and on the following day there was marked urinary frequency, hematuria, considerable pus in the urine, frequency and bloody urine existing for some two days; these symptoms subsided on the third day, when the urine became clear, only a few pus-cells being discernible in the specimens under the microscope.

Diagnosis.—Metastatic, embolic suppurative focus rupturing in the pelvis, initiated by chills, a complication of a staphylococcus abscess on the dorsum of the foot, associated with lymphangitis, there being at no time any symptoms referable to the kidneys, bladder symptoms predominating.

It will not be necessary to dwell here upon the various ureteral lesions that may simulate cystitis, for these are, as a rule, not difficult to diagnosticate, particularly the presence of ureteral calculi.

Callous Ulcer Simulating Cystitis

Among the bladder lesions, however, there is one which may be overlooked when patients are not given the benefit of careful cystoscopic examination, namely, that most distressing ailment, *callous ulcer* of the bladder. This is a lesion which may remain unrecognized for years, but which should be suspected in those

cases of intractable cystitis occurring particularly in young women, where tuberculosis of the kidney or bladder can be excluded. In several such cases that have come under my observation a most remarkable and rapid cure was effected by the removal of the ulcer-bearing area with the punch forceps through the operating cystoscope. The history of one such case will be presented here:

CASE XI.—B. S. consulted me November 21, 1912, because of an intractable cystitis, severe pain on micturition, and ardor urinæ.

Her bladder symptoms began in November, 1911, when she noted that she had to void more frequently than ever before, and that the act of urination was accompanied with burning and pain. At first she paid little attention to these symptoms until they became so severe toward the end of her pregnancy that she sought the advice of a physician, who prescribed internal medication. After her confinement in May, 1912, the symptoms did not abate, but gradually became more severe, so that she had to urinate every hour or less during the day and frequently during the night. In August, 1912, about nine months after the onset of her illness, she sought the advice of Dr. K., who found that the urine contained a large amount of pus and some blood. She remained under treatment for almost four months, receiving frequent vesical irrigation with silver nitrate without improvement. The dysuria, painful micturition, and increased frequency persisted, so that finally she was compelled to void as often as every fifteen or thirty minutes during the day and every fifteen or thirty minutes during the night. At times the urine seemed to contain clots of blood. Lately the pain was so severe that she would "double up" during the act of micturition.

On November 21, 1912, cystoscopic examination was made. The whole trigone was markedly inflamed, the changes on the right side being more intense than on the left. The left ureter could be detected as a markedly swollen orifice embedded in edematous mucous membrane. Not far removed from the left orifice occupying the middle and right cornu of the trigone there was a large whitish polypoid mass of exudate, the surface of which presented areas of brownish and blackish discoloration, giving the impression of a tumor mass about the size of a hickory nut (Fig. 214). The right ureteral orifice could not be discerned, it being evidently hidden by the mass. Far back in the bas fond, situated somewhat to the right and the median line, there was a superficial defect in the mucous membrane, and not far removed

from this in the posterior wall another smaller abrasion. The rest of the bladder appeared to be pale and almost devoid of changes. The presumptive diagnosis after this examination was chronic ulcer involving the region of the right ureter and trigone, with intense trigonitis, cystitis with some superficial defect, and possibly right renal tuberculosis.

The urine contained a large amount of pus, numerous red blood-cells, and cultures showed Staphylococcus albus. No tubercle bacilli could be found.

On December 6th she was again examined (without general anesthesia), the vesical changes being very much the same as those noticed at the last examination. Clear urine was obtained from both kidneys, the right side excreting 1.7 per cent. urea, the centrifuged specimen containing a few epithelial cells and a few white blood-cells. The left ureteral specimens contained 2 per cent. urea, microscopic examination showing a very few red blood-

Fig. 214.—Callous ulcer (2 cases).

cells. Both specimens contained a very faint trace of albumin. The cultures from both sides were sterile.

The findings at this cystoscopy, therefore, were the absence of renal involvement, the presence of a chronic ulcer in front of the right ureteral orifice, and cystitis with an area of erosion.

On December 8th a catheterized bladder specimen again showed numerous staphylococci (Staphylococcus albus) and an unidentified Gram-positive bacillus. No tubercle bacilli were found. A twenty-four-hour specimen also proved negative for tubercle bacilli.

Excision of the Ulcer.—With the diagnosis of chronic ulcer covered by a tumor-like exudate now well established, and with the striking curative result obtained in a previous case in mind, it was determined to excise the whole ulcer area and the polypoid mass by means of the punch forceps through the operating cystoscope.

Therefore, on December 8th the whitish polypoid mass was

completely removed and the base of the ulcer punched out, both soft and hard pieces of tissue being obtained. The margins of the ulcer and a fairly large firm fibrous piece (undoubtedly representing the bottom of the ulcer) were identified both macroscopically and microscopically. All of these pieces were sent to the pathologic laboratory for histologic examination.

On the day following the procedure the patient already gave evidences of improvement as far as the urinary symptoms were concerned. Three days later the improvement was already marked, the patient being able to hold 10 ounces of urine without trouble. The urine obtained by catheter was almost clear, contained a few red blood-cells and a few white blood-cells.

On December 19th, ten days after the excision of the ulcer, cystoscopic examination showed a complete absence of the ulcer. The right ureter was now distinctly visible, the trigone just in front of it being occupied by several small ecchymoses. The mucous membrane was swollen and the ulcer evidently in a process of rapid repair. The catheterized specimen of urine was perfectly clear and the patient regarded herself "well," voiding only three times during the day and not at all during the night. There are absolutely no vesical symptoms.

Cystoscopy, January 10, 1913, *revealed a practically normal bladder, there being no vestige of the ulcerated area.* Pale mucous membrane in front of the right ureteral orifice was the sole indication of the former lesion. *The patient considered herself "cured."*

Cases of this sort are beautiful examples of the value of exact diagnosis in bringing about a cure of otherwise practical hopeless affection.

Another interesting lesion which is frequently overlooked is solitary superficial ulcer of the bladder. Upon close investigation of some of the cases that come to us suffering with terminal hematuria and cystitis there will be found a small *superficial ulcer* somewhere in the posterior wall or roof of the bladder. Such superficial ulcers do not require the radical treatment of excision except in rare instances. Some of them respond to mercury injections, others to the high-frequency treatment.

Lesions of the Bladder Neck.—Because the fibrotic condition, the so-called contractures of the neck of the bladder and median bars, as well as fibroses of the prostate giving similar symptoms,

are so often confused in their clinical manifestations with "cystitis" it may be well to dwell for a moment upon this interesting pathologic change.

By the general term *contracture of the neck of the bladder* I wish to designate all those pathologic lesions involving the region of the internal sphincter and adjacent supramontane and posterior urethra, that result in the production of a greater or less coarctation of this portion of the urethral canal. The pure new growths, particularly adenomata, that may be located in the same territory, belong more properly to the class of cases known as hypertrophy of the prostate or adenomata of the prostate, and when they are unaccompanied by inflammatory or fibrotic lesions leading to a stenosis of the sphinteric region will not be regarded as belonging to the class of contracture of the neck of the bladder.

It was the pathologic study of cases that gave the clinical symptoms of contracture of the neck of the bladder, cases that did not belong to the class of adenomata, that led me to adopt a more extensive operative procedure, than those which merely have for their purpose the removal of a small portion of tissue from the floor of the sphincteric region, as described by Young. These pathologic investigations on material obtained by a wide exsection of tissue from the affected region led me to the conclusion that, although no single lesion is characteristic for all cases, and although a combination of lesions may occur to make up the complex of contracture of the neck of the bladder, nevertheless the anatomic alterations which produce the narrowing of the bladder outlet are so extensive and deep that a more radical surgical procedure should be followed by better results than some of the methods applied heretofore.

My own pathologic studies have brought to light that we are dealing with a combination of lesions in some cases, single lesions in others, always, however, representing invasion of the tissues situated at some distance from the mucous membrane side of the sphincter. These lesions may be a simple fibrosis showing no signs of previous inflammatory process, although such may have been present, fibrosis being superficial or deep, or there may be a fibrosis accompanied by an inflammatory process; or there may

be an inflammatory lesion involving the mucous side of the sphincteric region extending downward for a variable distance into the surrounding tissue or muscles, forming an inflammatory and fibrosclerotic sheath of varying thickness; or there may be a diffuse adenomatous invasion of the sphincteric region with or without periacinar inflammation, accompanied by more or less fibrosis. And finally, there are the mixed forms in which any

Fig. 215.—Region of the fibrotic sphincter (contracture of neck), showing tenaculum forceps elevating the floor of the sphincter before excision, according to the author's operative method.

of the above changes may be accompanied by accidental formation of precocious adenomata or fibromata.

Clinical Examples.—When a young or middle-aged man comes to us with a story of frequency of urination, either with clear or cloudy urine, *who is said to have had cystitis*, or who may have been regarded as a neurasthenic if his urine be negative, let us refrain from making the diagnosis of either neurasthenia or cystitis until we have carefully ruled out the possible existence

of *contracture of the neck of the bladder*. Too many young men are being daily designated as neurotic, and just as many cases with this same lesion are being regularly treated for cystitis.

Nocturia, diurnal increased frequency, urgency, irritative phenomena in the region of the perineum, indefinite and vague pains in the hypogastrium, particularly when the bladder is full, are the chief clinical symptoms. As the disease progresses, however, secondary cystitis and not infrequently calculous formation, and even later infection of one or both kidneys with either pyelitis or pyelonephritis are observed.

By means of an operation suggested by the author some two years ago a great number of these cases can be cured, but require the services of the experienced urologic surgeon aided by the application of the cystoscope, cysto-urethroscope, and universal urethroscope to make a differential diagnosis (Fig. 215).

Prostatic Lesions.—It should not be a difficult matter to keep in mind the various lesions of the prostate, such as the inflammatory, the neoplastic and intraprostatic calculi, that may give rise to confusion when the symptoms of cystitis present themselves. The rôle of the prostate is being fairly well recognized by the practitioner, and it may not be necessary to dwell for any length of time upon this phase of differential diagnosis, any further than to allude in brief to an interesting example of one form of prostatic infection giving symptoms of cystitis that are not so well known.

Metastatic Infection of the Prostate, Periprostatitis, Perivesiculitis, Complicating Small Inflammatory Bone Focus.

CASE XII.—J. K. was said to have had an infection at the elbow, presumably an infection of an olecranon bursa, which was incised, pus having been evacuated in April, 1916. A persistent sinus followed, which did not heal in spite of a number of curetings.

August 26, 1916, the inflammatory focus was seen to extend well into the olecranon, there being bone necrosis. In spite of thorough curetage the wound did not heal, but on September 29th there were symptoms suggestive of metastatic involvement of the right kidney, pain in the right hypochondrium and right lumbar region, high temperature, and pus in the urine. At the same

time there were symptoms of cystitis, urinary frequency, urgency and pain on urination, the prostate being tender, enormously swollen, and the region of the vesicles somewhat indurated.

Retention of urine occurred, catheterization being necessary for several days, the prostate being softer in places, so that it was possible, after a week had elapsed, to express some pus through the urethra on prostatic massage.

It was not until the infection of the kidney, periprostatitis, and perivesiculitis had abated that all the urinary symptoms disappeared.

Urethral Lesions.—The rôle of gonorrheal urethritis in the production of the symptoms of cystitis is so well known that no further account need be given here, an interesting case of infection of the kidney and ureter having been previously described. Strictures of the urethra of large caliber may be overlooked, when these are, in truth, responsible for the symptoms of or the development of an actual cystitis.

Calculus in the Posterior Urethra when Lodged Behind the Verumontanum, Having Been Passed from the Ureter, May Reside There for Weeks or Months Without Being Recognized.

Case XIII.—E. P., male, consulted me October 15, 1916, with the *diagnosis of cystitis*. He had had urinary frequency and the usual symptoms of cystitis, also difficulty on voiding for about one year.

Examination of the bladder with the cystoscope at once suggested the previous passage of a ureteral calculus. The evidences of enlargement of the left ureteral orifice, with slight suggestion of edema about this orifice, were sufficiently characteristic to warrant the careful search for a calculus, and since this was not in the bladder, and there had been no history of the passage of a stone, the posterior urethra was carefully inspected with a cystourethroscope, and a ureteral calculus found lodged in the fossula, just behind the verumontanum. It was an easy matter, therefore, to dislodge this, push it back into the bladder, and remove it with the author's punch forceps through the operating cystoscope.

This patient, therefore, who had been suffering with a so-called cystitis for about a year, was cured at one sitting by the application of the proper methods of diagnosis and treatment.

Extravesical Lesions.—Finally, let us pause for a moment to consider just a few of the very many extravesical causes for the symptoms of cystitis, for most of these are within the power of the practitioner to recognize, without the aid of a specialist. A routine vaginal or rectal examination, so often neglected by the busy internist, cannot fail to reveal the existence of a pelvic exudate, enlargement of the uterus, fibromyomata, ovarian tumors, carcinoma of the rectum, conditions so often responsible for the symptoms of cystitis, often not sufficiently characteristic in their manifestations to be recognized without careful palpation.

Even strangulated hemorrhoids or thrombosed hemorrhoids may give us the picture of cystitis, the latter failing to respond until a radical cure by operation is carried out.

Bladder symptoms may be the first clinical signs of the existence of a large fibroid of the uterus, or even of the existence of a pelvic exudate of tubal origin, that has been running a subacute course.

CONCLUSIONS

Let us sum up by emphasizing once more that numerous other pathologic conditions must always be borne in mind before the diagnosis of cystitis is made; that the catheter be applied early in the case of the female when the symptoms are those of so-called cystitis; that the future therapy, saving that which must be applied during the first days of acute symptoms, must not be decided upon until an exact anatomic diagnosis will have been made possible; and that the application of the cystoscope is certainly not dangerous in the chronic conditions, and should even be applied in the acute cases after the most severe stage has been passed. *With the proper agnostic attitude toward the nature of "cystitis" on the part of the practitioner, and a more intense desire to attain an exact anatomic diagnosis, much suffering will be prevented and the lives of some patients may be saved.*

CLINIC OF DR. HENRY RAWLE GEYELIN

PRESBYTERIAN HOSPITAL

CERTAIN ASPECTS OF THE MODERN TREATMENT OF DIABETES MELLITUS

WE will take up today the presentation of a subject which has received much attention during the past five years, namely, the treatment of diabetes. In other lectures and clinics you have had the general aspects of diabetes presented, and you have had the opportunity to see cases in the dispensaries and hospital wards, I therefore assume you are reasonably familiar with the theories of etiology, the symptomatology, and—to a certain extent, perhaps, with the treatment—of this very important disease.

When Dr. Allen advanced the principles underlying his methods of treating diabetes, which are now so universally accepted, there were two fundamental features that were original; one was the use of the fasting, or very low caloric period, to overcome acidosis and glycosuria; and the second was the demonstration of the insidiously harmful effect of a long-continued diet high in fat.

Those of you who have seen the diets administered in the wards of this hospital, and have also read about the diets recommended in some of the older text-books dealing with the treatment of diabetes, have probably wondered why the present-day diets contain so much less fat and proportionately higher amounts of carbohydrate. The reasons for this I will take up later, but first I want to indicate to you in a general way the line of treatment that should be followed when a patient first presents himself, in the early stages of the disease.

I can best illustrate this by showing the patient, whose history is as follows:

CASE I.—The patient, a girl aged twenty-five, single, first came under observation six weeks ago. She had suffered from

all the usual symptoms of diabetes for a period of two months, and had lost 15 pounds. She had gone to a physician two weeks after the onset of her symptoms, and he, without testing her urine, told her she was suffering from "weakness of the bladder," and gave her some "brown medicine." The symptoms increased in severity, she became much weaker, continued to lose weight, and was eating large quantities of any food she pleased.

The first day in the hospital, on a general and unrestricted diet, she showed 86 grams of sugar in the twenty-four-hour period. There was a ++++ diacetic reaction; the Blood Sugar was 0.22 per cent., and the Blood CO_2 was 43 volume per cent. The subsequent course can best be followed by means of the chart.

Date.	Twenty-four-hour urine.		Food. Grams.				Weight.	Blood Sugar. Per cent.	Blood CO_2 Vol. Per cent.
	Sugar. Grams.	Diacetic.	COH.	Protein.	Fat.	Calories.			
Jan. 3	86	++++	200+	90+	150+	2584+	125	0.22	43
" 4	24	++++	50	50	50	1075	..	..	..
" 5	18	++++	15	25	25	396	124	..	..
" 6	12	++++	0	0	0	0	..	..	..
" 7	5	++	0	0	0	0	125	..	..
" 8	0	+++	0	0	0	0	..	0.12	58
" 9	0	++	10	20	20	309	127	..	..
" 10	0	++	15	30	30	464	..	..	..
" 11	0	+++	15	30	30	464	127	..	..
" 12	0	++	20	40	40	618	..	..	..
" 13	0	++	25	50	50	773	125	..	..
" 14	0	+	35	60	60	948	..	..	..
" 15	0	0	35	70	70	1082	124	0.19	65
" 16	+	0	40	80	80	1236	..	..	..
" 17	0	0	0	0	0	0	..	..	..
" 18	0	++	20	60	60	888	..	..	..
" 19	0	+	25	80	80	1075	..	..	..
" 20	0	0	25	90	90	1309	..	..	..
" 21	0	0	25	90	90	1309	120	..	..
" 22	+	0	25	90	100	1402	..	..	..
" 23	0	0	0	0	0	0	..	..	..
" 24	0	0	25	90	90	1309	..	..	..
" 25	0	0	25	90	90	1309	..	..	..
" 26	0	0	25	90	90	1309	..	0.11	63
Discharged five days later on a diet of									
	0	0	40	90	90	1370	119	..	..

You will notice on the chart that the diet of the second day was 50 COH, 50 Prot. 50 Fat, and on the following day it was reduced to 15 COH, 25 Prot. 25 Fat; while on the fourth day a complete fast was instituted, which after three days rendered the patient sugar free. The first food after the fast was 10—20—20. The exact amounts were more or less arbitrarily chosen, and 5—10—10 or 5—20—20, or 15—30—30 might have been equally suitable. Now the next question is, How shall we increase this diet in order to determine what food the patient can take eventually and remain sugar free? Experience has taught us that a gradual daily increase from the beginning of all three foods in small amounts is the most satisfactory method in the average case. Some patients, of course, immediately after the fasting period are not able to tolerate as much as 10 grams of COH when given without any other food; while others tolerate as much as 30 COH, 60 Prot. 60 Fat the day after the fast. These figures, of course, represent extremes, but in the early days of treatment, that is, when the patient has been made sugar free for the first time, there is no definite way to determine in advance just what the immediate tolerance for food will be. The Blood Sugar is usually the best guide, but this is not always reliable unless we do repeated Blood Sugar determinations on the first feeding day, a procedure which is not always practicable, nor is it necessary.

You will notice in this case that the Blood Sugar was 12 per cent. on the first day following the fast. This suggested that the diet could be increased rather rapidly and, as shown in the chart, this assumption was correct; for after eight days in which the diet was increased daily, a tolerance of 40—80—80 was reached when sugar reappeared in the urine. The Blood Sugar at that time being 0.19 per cent. A second fast day was then given, and a diet of 20—60—60 followed. This lower diet, in turn, was increased to 25—90—100 when sugar reappeared, and then following the next fast day 25—90—90 was tried. On this the patient was sugar free for three days. Then following a gradual increase of COH (5 grams per day), keeping the Prot. and Fat

at a constant level, a food tolerance of 40—90—90 was attained; on this diet the patient was discharged.

She returns to the hospital today having kept this diet for the past two weeks and having taken one-half diet day once a week according to directions. She has not shown sugar or diacetic in the urine since her discharge and her weight is stationary. We will now instruct her as to her future treatment.

What guide have we in telling her whether or not

1. To increase the diet?
2. To keep the same diet? or
3. To decrease the diet?

MR. P.: The Blood Sugar will help, as will also her weight.

DR. GEYELIN: Yes, and the Blood Sugar has been done. It is 0.125 per cent. (four and a half hours after her last meal), which was breakfast. With such a Blood Sugar, and the weight far below normal, it is probably safe to give a slight increase in the food. How much would you give? and what food or foods would you increase?

MR. R.: I should think she needed more calories, and a slight increase in the fat would be the best way to give it—say 10 grams.

DR. GEYELIN: That would probably be the most advisable. But why not increase the protein or carbohydrate?

MR. R.: The patient is now receiving more than 1½ grams of protein per kilo body weight, and, as I understand it, this is the most generally accepted quota of protein for adults on a mixed diet. As for the carbohydrate, it seems to me that the patient is receiving enough for the time being in view of her original low carbohydrate tolerance and the present Blood Sugar level, which is at the upper normal limit (fasting).

DR. GEYELIN: Yes, I think that is good reasoning; because an increase of 10 grams COH would be more apt to cause glycosuria during the next two weeks than would an increase of 10 grams of Fat during the same period, and yet might it not be possible to give 5 or 10 grams more of COH?

MR. R.: Yes, sir.

DR. GEYELIN: Some might think it best to give even more of

an increase than we have suggested, but experience teaches us that gradual small increases in the food with the consequent probability of keeping the patient continuously sugar free, particularly during the early months of treatment, is the best procedure. By this method it has seemed to me that the patient is more likely to feel better; more likely to gain a better tolerance eventually, and, further, it is stimulating to the patient's morale to see a steadily increasing diet without the reappearance of sugar. Of course, you must all remember that if the body weight is falling off rapidly and the patient is getting weak, in spite of restricted activities, the diet must be increased more rapidly; as this additional loss of weight in itself may be the indication of a diet too far below the patient's tolerance.

The question of whether or not to leave this patient's food as it is, or to decrease the present amount, it seems to me is answered by the foregoing discussion. In other words, when a patient has been taking a given amount of food without showing sugar for two weeks or more, and the Blood Sugar continues to be normal or nearly so, and there is no gain in weight, there is certainly no danger in increasing the food as long as the patient is under proper supervision. This supervision should continue at two-week intervals for many months. In the more severe cases patients should return at least once a week to have their food intakes regulated. Before dismissing this patient there are several other details of the treatment that demand attention.

Some of you may have wondered why, on the first day of the patient's stay in the hospital, we allowed her to continue on a full diet. This, of course, would not be permissible if there had been any dangerous symptoms, such as those of marked acidosis or of oncoming coma; but there were none, and, as I will show you, we gained much useful information by observing how much sugar was excreted in twenty-four hours when the patient was eating the amount of food shown by the first figures on this chart.

Let us assume, for instance, a much more severe case of diabetes, one who on a diet of about 150 grams COH is excreting sugar in amounts exceeding 200 grams daily; this would indicate a negative COH balance, and the probability that sugar was

being formed from some other source than the COH of the food. That is, either from stored COH, which is not likely, or from food and tissue protein. This negative COH balance in itself is presumptive evidence of a more severe form of diabetes than the case I have just shown you.

You have probably also wondered why we did not put the patient on a fast period immediately. The reason for not doing so was that occasionally, particularly in diabetes complicated with nephritis or obesity, if a fast is initiated at once there is danger of causing acidosis, or increasing an existing one; so that a gradual reduction of the food to the point of actual fasting is the safer routine measure. Dr. Joslin, who has had great experience in the treatment of diabetes, believes in the following routine method of reducing the original high diet to the fasting level: On the first day "omit fat, after two days omit protein, and then have the carbohydrates daily until the patient is taking only 10 grams, then fast." This method of reducing the diet requires more time, and has no marked advantage in other respects over the method shown on this chart; furthermore, I have never seen any unfavorable results when the food was reduced in the manner I have shown you in the chart. The important underlying principle being not to plunge the patient from a high fat diet into an immediate fast day.

During the first part of the clinic today I told you that one of the most valuable contributions to the treatment of diabetes that Dr. Allen has made was his study of the ill-effects produced by long-continued high fat feeding, particularly when the carbohydrates were reduced to what was formerly termed the "carbohydrate-free diet." This so-called carbohydrate-free diet usually consisted of 10 to 20 grams of carbohydrate, 80 to 150 grams of protein, and from 150 to 250 grams of fat. It is quite true that on such a diet patients often remained free from sugar for periods ranging from many weeks to many months; but without any further change in the diet they then began to show sugar in increasing amounts. This was usually foreshadowed clinically by general languor, weakness, distaste for food, sometimes with actual nausea and diarrhea. There were pains in various parts

of the body, particularly in the extremities, and sometimes periods of unusual drowsiness.

If at this stage the patient consulted his physician, it was usually found that small amounts of sugar were present in the urine or there might be no glycosuria. In either case, however, traces or considerable amounts of diacetic acid were to be found in the urine. Not realizing the real significance of what was happening, namely, that the patient was getting too much fat, the physician, as a rule, increased the carbohydrate because of its antiketonuric effect, but maintained the fat intake at its previous high level. This procedure, of course, immediately caused an increase of the Glycosuria and temporarily decreased the amount of Diacetic Acid excreted. Intermittent periods of "green days" and in some instances "oatmeal days" were resorted to for the purpose of decreasing Glycosuria, but a return to the high Fat diet invariably followed, and this, in turn, increased the ketonuria. The underlying principle of treatment that prevailed at that time was that the patient's nutrition must be maintained at any cost and that he must not be allowed to lose weight. How false this theory was can be seen from the very unfortunate results that followed such treatment, particularly when contrasted with the very favorable results obtained with our present methods.

Nowadays, in such a case, armed with the experimental proof of the harmful effect of high fat diet on the diabetic, we take the Blood Sugar which, under these circumstances, is invariably high, and with it there is almost always a lowering of the Blood CO_2. Immediate reduction of the fat, followed by a period of fasting, or at least a period of low diet, especially one low in fat, will in time lower the Blood Sugar, raise the Blood CO_2, and render the patient free from sugar and diacetic acid. Frequently this takes many weeks to accomplish, and during that time it will be found that the tolerance for all foods is much lowered.

I will now show you a case which I think aptly illustrates the beneficial effects of modern treatment. This patient was suffering from a prolonged period of a diet too high in Fat.

The patient, a man aged forty-eight, first came for treatment in October of the past year (1917). He had had diabetes for two years previously. Up to June, 1917, he had treated himself. He then went under the care of a physician, who found that he had a good deal of diacetic acid and sugar, together with a high Blood Sugar. He was immediately put on a fast, which rendered him sugar free; the diet was then slowly increased until he was eating approximately 60 grams of carbohydrate, 100 grams of protein, and 180 or more grams of fat, and was still free from sugar. For one month on this diet he did well. He was free from sugar and gained slightly in weight and strength. The Blood Sugar remained normal. Shortly after this, in August, he began to feel "good for nothing." He would often sleep the greater part of an afternoon, felt weak, began to lose a little weight, and also had considerable pain in his legs and feet, particularly at night. Finally, in September, he began to have traces of sugar in the urine. He at first took fast days to clear this up, and then, as he was feeling worse, he began to eliminate glycosuria, when it occurred, by reducing the carbohydrate alone, leaving the fat and protein at their usual level. He did this repeatedly for two or three weeks, and then began to feel badly, was weak, had much pain in his feet, and for the first time he began to notice that his eyesight was rapidly failing. It was at this time (October, 1917) that he first came to the hospital for treatment.

As soon as he came under treatment it was found that his Blood Sugar was over 0.2 per cent., that his Blood CO_2 was 40 volumes per cent. He was excreting considerable traces of sugar in the urine, and had a ++++ diacetic reaction. The accompanying chart shows the progress of the case as far as the intake of carbohydrate, protein, and fats are concerned, together with the Blood CO_2, the Blood Sugar, and the weight.

It took more than three months before any change was noticed in his clinical condition; in fact, at first he grew weaker and his eyesight became more dim. His tolerance was increasing very slowly from a very low level, but was not nearly as high as it had been during the preceding summer. The only improve-

ment was that he no longer had pains in his legs and feet. In spite of the reduction of the fat, he apparently could tolerate no more carbohydrate than when he was getting a high fat diet. For the past four weeks, however, he has been steadily improving, he is much stronger, takes more interest in life, and his eyesight is much better; in fact, he says that it is almost as good as before the dimness of vision began. He can now tolerate 65 grams of carbohydrate, and this with a low Blood Sugar.

The immediate treatment instituted was as follows, showing the urine and food of the last day (October 16) before treatment was begun:

Date.	Twenty-four-hour urine.		Food. Grams.				Weight.	Blood Sugar. Per cent.	Blood CO_2 Vol. Per cent.
	Sugar. Grams.	Diacetic.	COH.	Protein.	Fat.	Calories.			
Oct. 16	22	++++	25?	100+	200+	2300+	141	0.28	40
" 17	20	++++	25	50	50	750	..	..	..
" 18	17	++++	10	30	30	430	..	..	..
" 19	5	++++	10	20	10	210	140	..	..
" 20	++	++++	0	0	0	0	..	..	..
" 21	+	++++	0	0	0	0	..	..	..
" 22	0	++++	0	0	0	0	143	0.17	52
" 23	0	+++	5	10	10	150	..	..	..
" 24	0	+++	10	20	20	300	..	..	..
" 25	0	+++	15	30	30	450	147	..	..
" 26	0	+++	20	40	30	510	..	..	..
" 27	0	++	20	40	30	510	..	..	..
" 28	0	+++	25	40	40	530	..	..	..
" 29	+	+++	30	40	30	550	..	..	..
" 30	0	+	0	0	0	0	140	0.15	58
" 31	0	++	20	40	20	420	..	..	..
Nov. 1	0	++	25	40	20	440	..	..	..
" 2	0	++	30	40	20	460	137	..	..
" 3	0	+	35	40	20	480	..	..	..
" 4	+	+	40	40	20	500	..	..	..
" 5	0	+	0	0	0	0	..	..	..
" 6	0	+	30	50	30	590	135	0.13	62
" 26	0	0	30	90	70	1110	138	1.3	65
Dec. 26	0	0	50	90	70	1190	138	1.4	60
Jan. 25	0	0	55	100	80	1340	137	1.3	60
Feb. 26	0	0	65	100	80	1380	136	1.2	60

I must supplement the figures in the chart by saying that once every two weeks during December, January, and February the patient received a routine fast day, whether there was glycosuria or not; also, that a half diet day was given when glycosuria appeared in the interval between fast days. In this case a half diet was always sufficient to clear up glycosuria.

What the eventual tolerance will be is hard to say, but judging from experience with similar cases it will probably be possible to raise the food to 80—100—120, and still keep the patient free from glycosuria. This may take several months, but if every precaution is taken we will probably reach this tolerance. A rapid gain in weight of 5 or 10 pounds, a steadily rising Blood Sugar, or an increasing acidosis will be the signal that we are increasing the diet too rapidly. In that case, and if it is impossible to get a higher tolerance than the present one, the patient must regulate his general activities to his caloric intake.

In other words, we must not force the calories upward simply in order to make it possible for the patient to lead a normal life. It is far better to let such patients understand that they are not normal, and that for the sake of possible eventual improvement they must live at a level of metabolism where the caloric output is commensurate with the caloric intake. A few cases do eventually show considerable improvement under this method of treatment, and certainly it is the only known method that offers any hope of ultimate success.

If we ever expect to improve, and perhaps in some cases cure, the pathologic condition that causes diabetes we must, first of all, keep our patients free from the first and cardinal symptom of the disease, namely, glycosuria.

It must be borne in mind that there a few cases where freedom from sugar is not practicable nor desirable. Such cases are, fortunately, rare, and they are the very severe diabetics where the diet necessary to keep the patient sugar free is so low that even with complete rest in bed the calories supplied by the food are not sufficient to prevent increasing weakness and rapid starvation. When this condition confronts one it is better to give sufficient food to maintain a moderate degree of

strength and allow the presence of sugar in the urine. The diet in such cases must be carefully watched and regulated so as to guard against severe acidosis and too great an increase of sugar in the urine.

Patients in whom such severe diabetes occurs are usually under thirty years of age, although older diabetics are not exempt.

CLINIC OF DR. JESSE G. M. BULLOWA

WILLARD PARKER HOSPITAL

LOCAL EVIDENCE OF TONSIL INVOLVEMENT IN THE CAUSATION OF DISTANT OR SYSTEMIC DISEASE

Significance of Focal Infection to Distant Disease. Case Reports: Deforming Arthritis with Renal Insufficiency, Mitral Stenosis and Infarct of Lungs: Chorea with Low-grade Fever, and Salpingitis. Criteria of Adequate Treatment. Enlarged Lymph-nodes and Other Stigmata of Absorption. Advantages of Local Anesthesia in Tonsil Operations.

So much has been written and so much evidence has been successfully adduced to show that the tonsils may serve as a portal of entry for general infections that the mere narration of additional cases will serve no purpose. The term "focal infection" has begun to take the place of the term "cryptic infection," and the word "cryptic" has reverted to its ancient meaning. Under this standard have been gathered many victories against chronic disease. This slogan, however, has not been popular in all quarters, and so long as it remains a catch-phrase that is not properly related to that ancient medical doctrine, *ubi pus, ibi evacuo*, it is bound to work havoc in the hands of routineers.

Much opposition has been aroused against the entire doctrine of focal infections as a result of unnecessary treatment or by imperfect treatment of a focus. Throats have been incompetently operated upon for tonsil infections, but the infection has not been eradicated, and then the procedure instead of its inefficient execution has been blamed.

The type of cases which illustrate what is meant by distant disease are the following:

1. Margaret F. came under observation at the age of twenty-three, having been bedridden with deforming arthritis for two years. Her jaws were partially ankylosed and she was extremely wasted. Her eyes were prominent and the backgrounds showed hemorrhages. The thyroid was slightly enlarged and there was universal enlargement of all lymph-nodes. She had a presystolic murmur at the apex of the heart. Her systolic blood-pressure was 200; there was urinary evidence of nephritis, and she had had hemoptysis. She was carefully studied at the City Hospital, where she died a short time later of a true renal insufficiency with a blood non-protein nitrogen of 240 mg. The autopsy revealed a tight mitral stenosis, evidence of former infarcts in the lungs, and kidneys shrunken to the last degree as the result of successive inflammatory invasions. The essential fact in the history was that at the ages of sixteen, seventeen, and eighteen she had been an inmate of one of the best hospitals in the city suffering from chorea, which was treated by the accepted methods. She had had frequent attacks of sore throat, but her tonsils had never been operated upon, and at the time of her later illness they were small and buried. In seven years this girl had been destroyed by successive invasions of her tissues from her focus, so that at the age of twenty-three she presented the appearance of advanced age clinically and pathologically.

Contrast this case with these others:

Alma H. had her tonsils operated upon inefficiently several times in childhood. At thirteen years of age she developed an acute chorea associated with an acute infection of the tonsil stump. After several weeks of unavailing treatment with salicylates and arsenic, the tonsils were enucleated by Dr. Henry L. Lynah. The chorea and the low-grade fever terminated within a few days, and there has been no recurrence of either in four years, in spite of all the conditions in the home and diet remaining unchanged.

Leonora A., sixteen years of age, at high school, was suddenly taken with a disabling attack of pain in the right lower abdominal quadrant and local symptoms of visceral inflammation, *i. e.*, muscle spasm and hyperalgesia, associated with a rise in tem-

perature to 102° F. Rectal palpation revealed an induration to the right of the uterus. Dr. Charles G. Childs, Jr., confirmed the diagnosis of salpingitis. From the very small tonsil stumps left after tonsillotomy under general anesthesia seven years previously pus could be expressed. The regional lymph-nodes were large, and each expression of pus from the tonsil was followed by slight aggravation of the symptoms for a few days, but with subsequent marked improvement lasting several weeks. Tonsillectomy under general anesthesia by Dr. Lynah was followed by complete and permanent cure of the condition, disappearance of the nodes, and cessation of the attacks of inflammation in the tube. When enucleated the tonsils were found to be much larger than had been anticipated, and they contained numerous discrete pus pockets.

These conditions may be explained either as due to the absorption of bacteria, which form infarcts, or by the absorption of the products of bacterial life or death, which act selectively and change the dispersity of the proteins in certain sensitized regions. There is another explanation possible, and that is, that the foci mechanically or chemically irritate the autonomic nervous system, thus producing distant changes.

Bacterial evidence has been relied upon by some as the criterion which shall determine surgical treatment of the tonsils. Clinicians of eminence have determined upon tonsillectomy, basing their judgment solely upon the result of cultures. To my mind, this is an unsafe guide, because we have learned at the Willard Parker Hospital to value more highly, for instance in the case of diphtheria, the clinical picture which is the body's response to the irritant than the mere finding of the Klebs-Löffler bacillus. Annually we see a number of cases in which antitoxin has been withheld too long from diphtheria patients because no diphtheria bacilli have been reported from the laboratory. And this in spite of the fact that the body itself, by its reaction, local and constitutional, should have demonstrated to instructed eyes the nature of the disease. Nor is the positive finding of diphtheria bacilli, even though virulent, a guide in the administration of antitoxin. The persistent carrier

state and the Schick reaction have demonstrated that diphtheria bacilli may exist in the absence of the disease diphtheria.

If this analogy is valid, it is worth while to inquire what is the local evidence of tonsil infection which may be associated

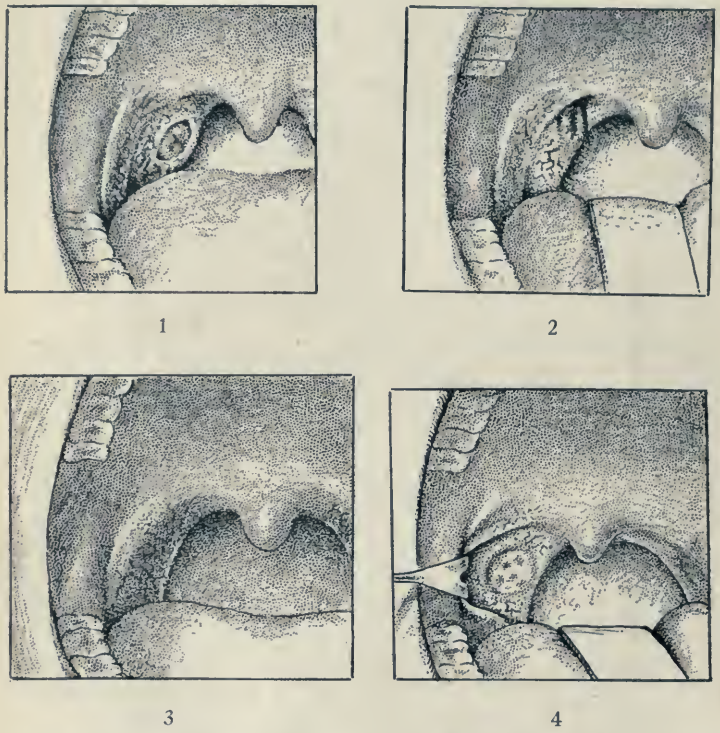

Fig. 216.—Types of diseased tonsil: 1, Diaphragm appearance of pillars which interferes with crypt drainage; 2, maldevelopment of lower tonsil segment, inflamed plica, with supraplical tonsil folded on itself and surfaces fused; 3, inflamed and prolonged mucous membrane fold which conceals tonsil even when patient gags; 4, small buried tonsil, which is only revealed when anterior pillars are retracted.

with distant or systemic disease. We realize that it might be, and to a certain extent is, possible to differentiate clinical pictures in accordance with the particular invading organism, but we have attempted no such refinement here. This problem has engrossed me for a long time, and it seems to be one that has

not received the attention it deserves at the hands of the medical profession. There is no special examination required of medical men which is more often performed perfunctorily than the examination of the throat. There are men who carry stethoscope and ophthalmoscope who draw inferences concerning the health of tonsils that they have never seen.

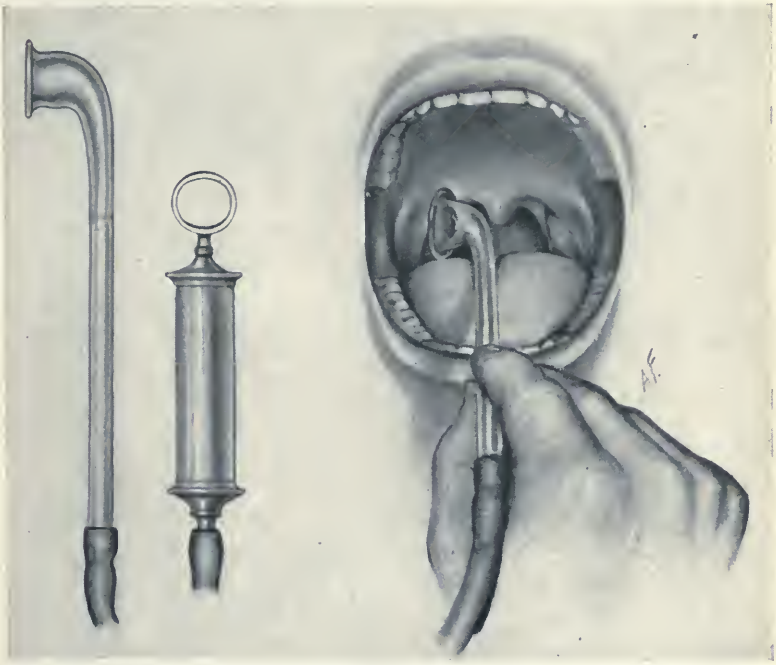

Fig. 217.—Method of determining condition of tonsillar crypts by suction with simple apparatus. Pus exuding from crypt.

The problem is one which more often confronts the internist and general practitioner than the nose and throat specialist. Patients who have sufficient local symptoms to seek the aid of the specialist independently have subjective evidence of the source of their trouble. They come, as it were, labeled.

These strictures on the usual examinations are made in spite of the improvement resulting from the popularization of the illumination of the oral cavity since the introduction of cheap and

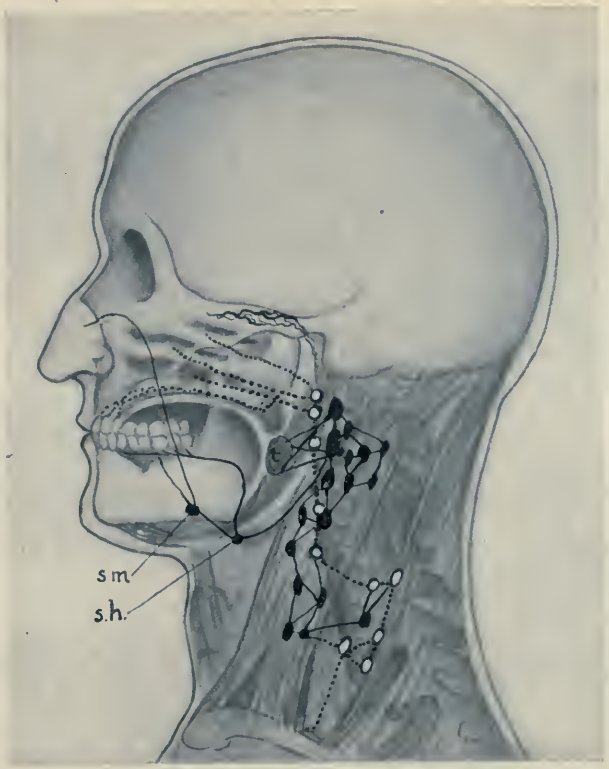

Fig. 218.

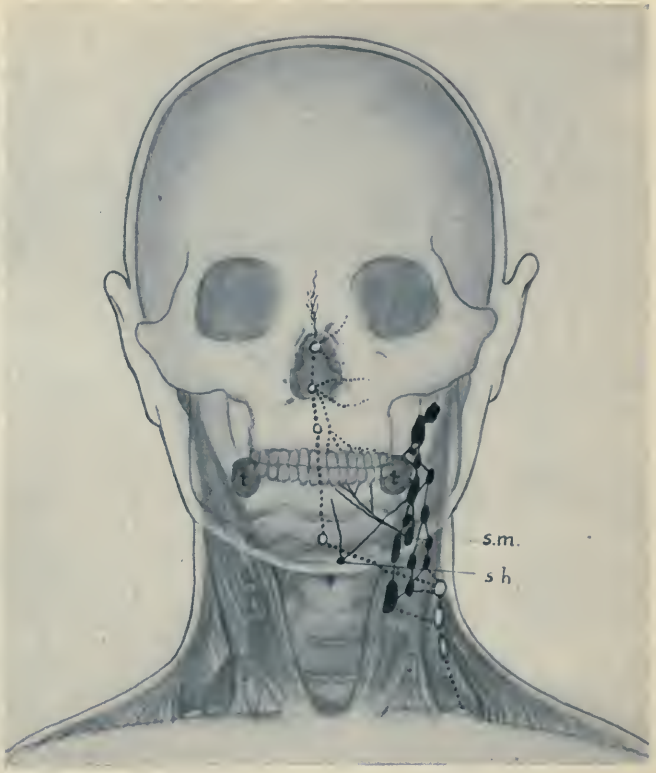

Fig. 219.

portable flash-lights. Frequently patients will report that they have been told that they have no tonsils, or healthy ones, when on questioning it is evident that it must have been impossible for the examiner to have seen the tonsils in his examination. The difficulty in viewing them may have been due to a high-standing tongue which was not depressed; or it may have been due in patients able to depress their tongues, and these have frequently been great garglers, to the fact that there had been a prolongation of the mucous membrane covering the anterior pillar so that it completely covers the tonsils. Such tonsils may be bent upon themselves so that the two surfaces are in contact. These surfaces may fuse if, as the result of irritating discharge, granulations replace epithelium (Fig. 216, 2).

Another type of buried tonsil is accounted for by the fact that the tonsil develops by the fusion of two portions, thus forming the plica or fold; where the lower segment is poorly developed or absent, the smooth plica may bury the upper developed portion. It is quite obvious that a view of the smooth plica may give little evidence of the condition behind it. To examine the tonsils it is necessary to see them and determine whether they are healthy and whether their crypts are emptied of detritus by the constrictor action of the anterior and posterior muscular pillars. The normal tonsil is easily emptied of detritus, and it is only when the plica fuses with the posterior pillar and forms a recess that there is retention in the upper crypts. At times the tonsil enlarges, but does not protrude between the pillars; they cover it like an iris diaphragm and retain the secretion (Fig. 216, 1).

Figs. 218, 219.—Anterior and lateral of main lymph drainage areas in the head and neck prepared from clinical studies: *t*, Tonsils; *s. m.*, submaxillary node; *s. h.*, suprahyoid node. Solid network above superior turbinal shows drainage with meningeal system, inosculating with retropharyngeal nodes. Dotted lines and white nodes show drainage of upper teeth, deep face extending to level of hyoid and then in posterior triangle. Solid lines and black nodes show drainage of tonsils, lower teeth, tongue, and superficial face. The deep and superficial chain both inosculate and empty into subclavian vein. The lymph-nodes of the tonsil are indicated to be superior and behind the tonsils, differing in this respect from the usual diagrams.

A type of tonsil which causes trouble is the so-called small cryptic or buried tonsil (Fig. 216, 1). I am frequently asked how it is that many people have had no trouble with their tonsils and nevertheless develop degenerative conditions at middle age which are attributable to them. There are two possible explanations: either the tonsils have been diseased for a long time and the systemic condition suddenly becomes sufficiently severe to attract attention; or, with the atrophy of lymphoid tissue incident to aging, the tonsils shrink so that they are no longer sufficiently large to be compressed by the pillars. In some throats the upper portion of the tonsil may be grasped and emptied, while the lower follicles may be the source of infection.

To view the tonsils properly requires a depression of the tongue, and in many cases the patients must be made to gag in order to throw the tonsils into the field of vision. The tonsils lie on the inner wall of the pharyngeal tube and do not naturally, in normal swallowing, face forward. Frequently, in order to expose the tonsil, it is necessary to retract the anterior pillar or the plica with a hook or retractor. No examination of the tonsils is complete unless the condition of the crypts has been determined. This can be done by suction or expression (Fig. 217), or by observing the destructive effect of irritating discharges.

When the head is slightly flexed the tonsils lie opposite the ramus of the jaw, and if, after the tongue is depressed, the tongue depressor is brought up against the pillars from below with pressure against the jaw, pus may frequently be expressed from the crypts and the supraplical pocket, into which some crypts may empty. There is no other way, to my mind, of determining whether the crypts on the superior aspect of the tonsil are emptied by the normal swallowing movements.

The inability to express pus must not be taken as evidence of its absence from crypts whose openings may have become occluded. Pus sometimes dissects its way into a pocket upon the capsule behind the tonsil. The absence of detritus is not evidence that the tonsil is healthy. The inflammation may be diffuse.

Several times I have seen tonsils which were described as sclerotic, and from the whitish mass which prompted the inference thick pus has been evacuated. Diseased tonsils may show either an increased redness and an increase in the lymphoid tissue overlying them, or they may show fusion of the pillars (and these are particularly deceptive), or there may be fusion of the tonsil with one or the other pillar. An irritating discharge from the crypts may destroy the epithelium about their orifices. The anterior pillars are frequently covered with a fine network of small vessels. If the patient has been unfortunate enough to have smoked, the condition will surely be called "smoker's catarrh."

The evidence of pus or, in other words, the evidence of infection of the tonsil is the same as that of infection anywhere in the body. The main reliance should be placed upon the evidence furnished by lymph-node involvement. The path from the tonsils to their regional lymph-nodes is not as long as that from the fingers to the epitrochlear or axillary lymph-nodes, nor is its path streaked with visible red. It is not as well known nor is its importance appreciated. A knowledge of the location and drainage areas of the neck is of very great importance as an aid to diagnosis, and is not sufficiently understood. (See Figs. 218, 219.) So important is the condition of the position of the lymph-nodes involved in infections about the head and face that its clinical significance cannot be overemphasized. By observing the regional lymph-node involvement patients will be preserved from many unnecessary *x*-ray exposures and directed to those which are necessary. The inference drawn from roentgenograms of the teeth should be fortified by clinical observation of the lymph-nodes involved. I shall digress for a moment to discuss the drainage areas of the face and throat.

The tonsils drain into the deep lymphatics of the neck which lie on the outer side of the jugular vein. When these are inflamed they are best palpated high up in the neck above the level of the tonsil, by compressing them against the transverse processes of the vertebræ with the thumb or index-finger (Fig. 220). They are to be felt in a triangle formed by the posterior belly

of the digastric and the sternomastoid muscles. They may be located best by palpating first the pulsations of the carotid artery. They are situated a centimeter or less to the outer side of the artery, for they rest to the outer side of or upon the jugular vein. The fingers may be hooked about the sternomastoid muscle and the nodes may be grasped between them if desired.

Fig. 220.—Method of palpating deep cervical glands with thumb against vertebral column high up in the triangle formed by posterior belly of digastric and sternomastoid muscles. These glands drain from tonsils, tongue, and lower jaw.

Frequently they are tender, and they may be followed down the course of the vein. The head should be slightly flexed, both forward and laterally, and turned to the side being examined during the maneuver (Fig. 220).

These deep cervical nodes drain the lymphatics from the face, tongue, and teeth of the lower jaw. If the face or teeth of

the lower jaw are involved, a gland situated just inside of the mandible and behind the groove of the facial artery is enlarged. If the mandibular or tongue area is involved, the so-called gland of the tonsil, or gland situated behind and below the angle of the jaw, is enlarged. In my experience it is the exception rather than the rule for this gland to be much enlarged in tonsillitis.

When the teeth of the upper jaw or the sinuses are infected the upper portion of the deep cervical chain usually escapes. These areas drain into retropharyngeal glands situated behind the pharynx, and thence into the lower portion of the deep cervical chain which lies under the sternomastoid muscle below the level of the larynx. This chain becomes superficial behind the sternomastoid, and sometimes, in order to protect it from pressure, the shoulder is raised, thus relaxing the muscle. These patients frequently complain of pain in the arm at the insertion of the deltoid as a result of the strain upon that muscle. The removal of pus from a point in the area whence they drain is frequently followed by very speedy relief of pain in the muscles of the arm. At times the retropharyngeal glands may be palpated when the larynx is moved aside and they may be visible through the pharyngeal wall; sometimes they are covered with adenoid tissue. The area above the uppermost turbinal bone drains with the meningeal system.

In discussing absorptions from the tonsils we have so far considered only such stigmata of absorption as may occur from the existence of pus at any point in the body, namely, lymphatic node enlargement, redness, swelling, tenderness, and pain. These patients may have frequent recurrent attacks of discomfort in the throat which they do not interpret as pain because the surrounding tissues are so unusually lax for the purpose of permitting free movement. But there are other local symptoms which are due to the fact that the tonsil is an organ; these are the referred zones of hyperalgesia.

For a long time I have been observing the areas of herpes associated with acute and chronic tonsillitis, and have come to believe that the popularly called "fever blisters," if they are situated at the vermilion border or slightly above or below it and near the

angle of the mouth, especially if external to the line of the philtrum which indicates the point of fusion of the nasofrontal and maxillary processes, are due to distensile pressure in some crypt in the tonsils. These herpes are preceded and accompanied by a hyperalgesic zone to pin scratch which is quite definite. If the skin is blanched by stroking with a pin or with the finger,

Fig. 221.—Location of herpes associated with distention of most superior crypts of tonsils (described in text).

the herpetic zone may be prefigured by dilated capillaries over the area corresponding to or prefiguring herpes.

These areas are the anterior portion of the tonsil zone, and I have learned to look at the upper portion of the tonsil for distended crypts when they occur upon the upper lip, and at the lower portion when they occur upon the lower lip. The posterior

PLATE 1

Herpes on lip associated with distention of upper tonsil crypts shown in Plate 2. On the right side of face, capillary dilatation in blanched area, induced by stroking lip with pin, corresponding to area of hyperalgesia and often prefiguring herpes.

Inflamed appearance of anterior pillars which frequently reveals a diseased tonsil.

Exposure of diseased tonsil by gagging and method for expressing pus from crypt emptying into the supratonsillar fossa.

PLATE 2

tonsillar area is the one usually figured; it is a small triangular zone which lies just posterior to and above the thyroid cartilage. Several times I have found a small area of herpes or of hyperalgesia on the cheek just above the nasolabial fold. This has been associated with a distention in the most superior crypt under the plica (Fig. 221).

The correctness of these inferences is also attested by the observation of cases in which herpes ceased to occur after tonsil enucleation, and by several cases in which the occurrence of lateral labial herpes was terminated by tonsil resection, but the philtral herpes continued to appear with subsequent maxillary inflammations.

The hyperalgesia sometimes comes into consciousness and is interpreted as neuralgia of the throat or face, but this must be distinguished from the recurrent attacks of pain in the ear which may be due to closure of the eustachian tube from edema, for these latter have the same basis as the recurrent colds in the head which occur in tonsillitis as the result of lymph stagnation, or stoppage brought about by the swelling of the lymph-nodes. I have had occasion to observe marked induration of lymph-nodes in a furuncle of the neck associated with congestion and increased discharge from the same side of the nose.

Let us enumerate the local symptoms of tonsil infection: Recurrent attacks of pain from distention or infiltration; redness and swelling of the tonsil and peritonsillar tissue, and I should add to these the evil or putrid odor which may be due to the growth of Streptococcus putridus or to decomposition of detritus; destruction of the tonsillar epithelium by an irritating discharge and its replacement by granulations; regional lymph-node swelling and tenderness which may occasionally cause blocking of other areas, as, for instance, the nose or eustachian tubes or larynx when the involvement extends down sufficiently to take in their drainage areas; and referred sensitiveness to pin scratch or hyperalgesia with a capillary dilatation which may be so severe as to manifest itself as herpes.

It is pertinent to remark that competent treatment of the tonsils requires that these local signs of tonsil inflammation shall

entirely disappear as a result of operation on the tonsil, and it has been my experience that where they have not been relieved the tonsil operation has been inefficiently performed and a small crypt-containing mass has remained in the upper pole or near the base of the tongue. This is especially disastrous if the tonsillar pillars have been mutilated during the operation. For example, a little girl had her tonsils removed by a competent operator who left a small segment in an upper pole. The indication for the original operation was frequent recurring colds in the head. The posterior pillar was cut away. Three years later the remnant of tonsil became infected and was the cause of a severe, acute polyarthritis which terminated abruptly when the remnant of tonsil was removed and about 1 c.c. of pus evacuated. This procedure was undertaken because of the persistent large and tender regional lymph-nodes and the redness and infiltration of the anterior pillar.

The results of the removal of infected tonsils are so brilliant that frequently the procedure should be offered to patients who are otherwise unfavorable anesthetic risks, for there are a number of advantages in local anesthesia for tonsil operations: The irritant action of the anesthetic on the lung tissue is avoided; there is no danger of the inspiration of infected material or blood with its attendant risk of lung suppuration or pneumonia; the danger of hemorrhage in an unconscious patient is avoided, as the patient can co-operate and give the alarm. In some diseases it is a serious matter to even temporarily change the physical state of the body lipoids. For the operator, the position of the patient is that in which the surgeon is accustomed to examine and the landmarks are familiar. The performance of the operation under local anesthesia requires a simpler technic, though a greater degree of dexterity, than under general anesthesia.

INFLUENZA OF THE HEAD AND CHEST

Outstanding Clinical Features. Stimulation from the Viewpoint of Colloid Chemistry. Individual Symptoms and Their Specific Management. Value of Special Drugs. Causes of Death and Valuable Prognostic Signs. Fallacy of Drastic Catharsis and of Forcing Fluids.

I SHALL not attempt at this time to discuss the prevention of infection by influenza, for testimony is very conflicting as to the value of various procedures. At this hospital we have relied upon the use of gowns and caps and careful washing of the hands after contact with the patients. Masks and cubicles were employed in a single ward only, but comparable data is difficult to obtain. All people are not susceptible to influenza and, as William H. Park has shown, any measures which are adopted after the peak of the epidemic has been passed will then seem to prove favorable.

As we observe the patients, the outstanding feature is their cyanosis or dusky complexion. Nearly every individual who suffers from influenza has a florid complexion. This was so pronounced in the first sailors that were brought ashore into this hospital in September, 1918, that they looked like mulattoes. It was also particularly noticeable in a company of marines who had enlisted from the northwest and who were the descendants of Scandinavians; their swarthy complexion contrasted sharply with their light hair and blue eyes.

It is not only the color which is characteristic of influenza patients, but the puffiness of the tissues; they seem congested. This reaction of the tissues seems to be due to the Pfeiffer bacillus. Some experiments which I performed at this hospital with the assistance of Dr. Skeers are interesting. We injected intracutaneously 1 or 2 minims of a vaccine of Pfeiffer's bacillus in several groups of cases. In susceptible patients, especially those

in the early stages of influenza, there was a very intense local reaction. The skin about the site of injection became swollen and violet colored within twenty-four to thirty-six hours, and frequently there was an accompanying enlargement of the regional lymph-nodes. Control injections of streptococcus vaccine in these patients gave at most a small pinkish area of infiltration. The influenza vaccine reaction was hemorrhagic and it persisted for a number of days and then subsided, leaving the skin stained. Though this does not by any means prove the etiologic relation of the Pfeiffer's bacillus to the clinical entity known as epidemic influenza, nevertheless the perfusion of the tissues with the poison of the Pfeiffer's bacillus and their reaction to it is a phenomenon which we have to treat in influenza. Miss Valentine's work on our patients has shown that many different strains of influenza bacillus are involved, and Dr. Park succinctly sums up the question when he says "the flu" permits the invasion of your own influenza bacillus. This changed condition of the reactivity of the tissues to an irritant is shown in the Schick reaction in one of the patients at this hospital who was very ill with a double bronchopneumonia. The injection of diphtheria toxin on the thirteenth day of her illness was followed by a necrosis of the tissues at the site of the injection. This patient subsequently recovered under the plan of treatment outlined in this lecture.

The local congestion which we have now discussed must be sharply contrasted with a cyanosis which has an entirely different cause. This cyanosis or fuchsia-colored appearance of the lips, seen in so many of these cases, is due to a congestion of the lung and emphysema and the consequent changes in the circulation in the head. This congestion is also present during the asthmatic phenomena of anaphylaxis or serum sickness. These two types of congestion, local and pulmonary, seem to me to be the determinative pathologic condition in the disease as we meet it and to give direction to our therapeutic attempts.

The occurrence of a local congestion is an edema phenomenon associated with a locking of fluid in the tissues. This fact must be kept in mind, for when the swelling state terminates

there may be a sudden release of fluid which may prove disastrous. The characteristic sweatings are evidence of the occurrence of free water. Like many colloidal phenomena the pectization or coagulation process does not cease at a medium state, but proceeds to such a degree that the patients appear emaciated. This local congestion determines by its localization many of the varying clinical aspects of the disease, and if the disease is viewed from this angle much of its protean character disappears.

Congestion and absorption from the nasal mucous membranes are responsible for the enlargement of the posterior cervical nodes. The local swelling in the nose accounts for the headache and nosebleed which are such frequent and distressing symptoms. If this swelling involves the uppermost recesses of the nose the drainage may be into the meningeal system and symptoms of a meningism may result. This was shown in a patient, a lad eighteen years of age, who, during the height of the epidemic, suddenly developed a temperature of 105.4° F., severe headache, retraction of the head, Kernig's sign, rigidity of the neck, and somnolence. This boy had obstructed nares, enlarged posterior cervical nodes, and marked deviation of the septum due to maldevelopment of the maxilla. The shrinking effect of adrenalin dropped into his nose caused the entire disappearance of the symptoms in eighteen hours.

At the Willard Parker Hospital it was a noteworthy fact that the only cases of complicating sinusitis occurred in Asians, who have very low nasal bridges and large frontal sinuses, or in men with narrow nasal passages. The use of adrenalin was of distinct benefit in preventing head complications and relieving headache; the zone of central forehead hyperalgesia disappears after adrenalin. The use of aspirin was rarely resorted to. The use of adrenalin had an additional rationale, as it seemed to prevent the absorption of toxin from the nose. Toxin carried in the blood may act in the presence of Pfeiffer's bacillus on the lung cells as a sensitizing agent and assist in the production of the local reaction we term "bronchopneumonia." The anaphylactic nature of this reaction is suggested by the late appearance of the phenomenon, usually six days or more after the head invasion.

Its sudden onset at times with all the phenomena of an acute asthma suggests the validity of applying to the human Manwaring's experiments on guinea-pigs as an explanation of this asthma. The congestion in the lungs most frequently involves the lower lobes.

The profound changes in the tissues induced by the disease seem to be associated with a clinical disturbance of the distribution of the lime in the body. This is manifested not only by the edema or change in the emulsion state, but by the following clinical evidence: changes in the menstruation; changes in the teeth; falling of the hair; the very marked response to stimulation with drugs, such as adrenalin and pituitrin which increases the power of lime utilization by the body; and, finally, evident loss of resistance to disease foci. There is further evidence of the lowered resistance in the greater susceptibility of individuals with lowered lime serum content, such as chronic alcoholics or hyperthyroids and pregnant women. The age incidence of influenza between twenty and forty may be accounted for by the fact that during that period the lime is being utilized in body metabolism.

These profound changes are evidently produced by some toxin. Physicians say that the patients appear "toxic." What they really mean is that they observe the poor perfusion of the capillaries of the face with slight swelling of the tissues. This may be induced by the action of a toxin upon the sympathetic nervous system. The peripheral circulation is poorly maintained during the course of this disease. The French writers, especially Sergent, have emphasized the importance of this phenomenon. When the skin is gently stroked over the abdomen or elsewhere, the stroke is followed by the appearance of a white streak instead of the usual red one of health. I have learned to pay great heed to the prognostic value of the occurrence of Sergent's sign, and it is a great relief to find it disappear after the use of adrenalin or pituitrin, for it is an evidence of the recovery of the sympathetic tone, and I have seen few patients recover where the white line has been persistently present.

The experimental laboratory evidence offered by Miss Parker,

a biologist at the College of Physicians and Surgeons, and Dr. Hatfield, of our laboratory, of the existence of a filterable toxin obtained from the Pfeiffer bacillus seems very convincing and should point the way to the production of an antitoxin.

These remarks lead me to a discussion of the methods which the body possesses to destroy such filterable toxins. It is frequently stated that a toxin may be removed from the body by lavage of the tissues. The crowding of fluids for the purpose of lavaging the tissues is a frequent practice. Possibly the toxin may be diluted by such a method, but the bacteria are by no means eliminated, and new toxin is constantly being produced. No intelligent physician would attempt to treat diphtheria, the symptoms of which are also due to a toxin, by crowding fluids. It has been definitely shown that the diphtheria toxin cannot be removed from the body after it is fixed to the tissues.

The disadvantages of lavage in influenza far outweigh the advantages. The tissues of the kidneys are damaged as well as the tissues of the circulatory apparatus, and the introduction of large quantities of a crystalloid (water) imposes a great strain upon both systems. Later in the disease, when the emulsion state in the congested areas is broken and there is a critical release of free water, it may be impossible for all the water to be absorbed and normally circulated. Indeed, the giving of large quantities of water may lead to a retention of the emulsion state with a resulting gelatinous condition of the tissues. Such a case came to autopsy at the Willard Parker Hospital, a man who had successive portions of the lungs involved in sequence. When autopsied on the twenty-eighth day of the disease the entire lungs were gelatinous.

Finally, the giving of large quantities of water causes of itself congestion and increased secretion of the lungs, as anyone who has observed the benefits of water deprivation in the congested lungs of cardiac disease may have observed. I have frequently seen attacks of faintness and coughing one hour after a meal or drink, which in such cardiac patients is equivalent to a stalling of their motor with fluid.

There are still other disadvantages from crowding water.

The lavage of the kidneys deprives the body of salts which it can ill afford to lose, and which may deflocuate protein and liberate toxin which had been absorbed earlier in the disease. The mechanism of detoxication in the body is by adsorption, precipitation, and oxidation. The toxemia of influenza may be met by reducing the absorption of toxin from the lung by diminishing the area of infected tissue perfused, by the use of adrenalin in the nose and mouth or subcutaneously, absolute rest in bed, and in certain cases by the performance of a partial pneumothorax by the method of W. Parry Morgan.

Precipitation may be accomplished by the introduction of convalescent serum as Redden, of Boston, has employed it, or by the introduction of the intravenous or subcutaneous use of various drugs or substances. At the Willard Parker Hospital I have been observing the results from the subcutaneous use of boiled milk with some apparently successful clinical results, which I attribute to the pectization or coagulation induced. It is possible that the apparent benefit in certain cases, after the early use of salicylates, is due to the coagulation of protein in changing the surface conditions in the blood.

Oxidation is favored by suitable methods in reducing congestion in the respiratory passages, such as the local application or subcutaneous use of adrenalin.

So serious a matter is the excess of free water in the body in influenza patients that it is safe to say it is responsible for many deaths. In fact, the majority of influenza patients die in one of two ways. Some drown in their own secretions, struggling for air, with an intact nervous system, but faulty heart and lungs. This manner of death may occur after the crisis of the disease when the temperature has become normal, and is largely due to the inability of the body to rid itself of water which is suddenly liberated. It should be forestalled by the limitation of fluids. Exception must be made in the case of children who do not stand water deprivation and whose tissues are naturally more turgid than those of adults and have a greater capacity for absorbing water in an emergency. These drowning patients are most pathetic, as they become more and more restless and realize their

inability to breathe. Phlebotomy is of little value in these cases because the removal of blood lowers the blood-pressure, especially in the coronary arteries. Deprivation of fluid increases the viscosity of the blood and raises the blood-pressure.

It is probably on this account that such marked variations in the prognosis of cases have been noted by many observers from week to week, as this may be conditioned by the gas tension in the tissues, which, in its turn, is the result of barometric conditions. These cases are at times temporarily relieved by the use of atropin and cupping. Pituitrin, which seems to increase the hydration capacity of the tissues, is useful if the amount of water to be taken up is not too great and it is given sufficiently early.

Many dying patients present another picture. These have a paralysis of the vasomotor system. They have a very low blood-pressure and their extremities are cyanosed and cold. The blood becomes pooled in the great vessels of the abdomen and frequently the more intelligent ones complain of a substernal anguish. That death is not due to failure of the heart is evidenced by its automatic action for many hours after the patients are unconscious. These patients have had their nervous systems damaged either as a result of blood deprivation or of the toxin. When the vasomotor system has been damaged for a relatively short time it does not recover, so that it is essential that the condition be promptly recognized. This may be done by careful observation of the patient, and I have learned to rely upon the symptom of irritability or wakefulness.

This wakefulness, if it cannot be relieved, is an omen of very sinister import. It may be explained as the result of poor circulation in the brain, or by the primary action of the toxin upon the nervous system. Patients who do not sleep do ill, and although I have seen such patients recover, it is only as a result of successful treatment, for their natural course is downward. Such patients may seem well oriented and apparently rational, but they become wildly delirious suddenly and may leave their beds and so exhaust the circulation. Such patients are the ones who show anxiety in their delirium, as well as cunning, treachery, and suspicion, and frequently assault their attendants. One such

patient, after three sleepless nights and days, started from his bed for the purpose of slaying his wife, whom he suddenly accused of trying to murder him, and when grasped by the attendant, exhausted himself with his struggles so that he died.

When the patients have come to this condition no treatment is efficacious. Sleep must be procured, and for this purpose the best drug is morphin, in $\frac{1}{4}$-grain doses hypodermically. Atropin should not be used in these cases because of its action on the capillaries, not only of the brain but of the skin. It increases the delirium. Occasionally we have used barbital (veronal) in small doses, but it is useless even as a symptomatic remedy in the more advanced cases. The action of morphin probably depends upon its selective action in increasing the utilization of lime by the nervous system. In certain cases the administration of 15-grain doses of precipitated chalk, four times a day, has aided in securing sleep. Some of the patients obtain sleep as a result of hydrotherapy, or from the improved circulation from digitalis. The prompt treatment of insomnia in influenza patients is indicative of a far-seeing and careful physician. Patients who have been somnolent have a better prognosis than those who are wakeful.

It is not my purpose to discuss the various ways in which influenza patients die, as this would require a separate discussion. At times foresight and watchfulness may prevent a tragedy; but unfortunately, as in the cases of singultus (hiccup) or of marked disturbance in the cardiac mechanism, I know of no remedy which will avert death. In the latter case irreversible colloidal changes seem to have been induced.

We have considered thus far the usual symptomatology of influenza involving the head and chest. We have not mentioned the mechanical difficulties associated with the acute pulmonary and tissue emphysema which are closely related as cause and effect. These conditions are amenable to mechanical treatment, the details of which I will discuss more fully at another time.

I have discussed at considerable length the fallacy of forcing fluids in influenza, and I have observed what seems to me an equally atrocious practice in the initial treatment of the disease.

I refer to the use of drastic catharsis, and especially the use of calomel. Mercury has a selective action upon the nervous system, and it seems hardly rational to add a mineral poison in the presence of a vegetable or bacterial toxin. The constipation which so frequently occurs at the onset of influenza is due to overstimulation of the sympathetic nervous system induced either by the primary invasion of the poison or by pressure from the swelling of the head mucosa. If no cathartic is given, the spasm relaxes and the bowels move. The justice of this view is borne out by the fact that diarrhea occasionally occurs. As the years have passed the catharsis at the Willard Parker Hospital has become less and less drastic in infectious diseases without detriment to the patients, and it is interesting to note that our mortality among our influenza patients was 8 per cent., whereas at a certain naval station, where according to official report calomel was a routine, the mortality was 20 per cent.

In patients whose bowels have moved with the invasion there is no advantage to be gained from purging. A mild laxative may be useful in the other cases. At times, as the result of relief of nasal pressure by the use of adrenalin, the bowels move spontaneously. Violent purging in acute disease is a relic of the practice which obtained when evil spirits were evacuated from the bowels; the larger the movement, the more *noxæ* was removed, and therefore the more drastic the purge, the better the practice. The practice of violent purging is on a par with the antipyretic treatment of fever.

A recognition of the fact that the influenza poison spends itself on the sympathetic nervous system leads to one other practice in the management of these patients. They should be kept absolutely at rest in bed. Many patients exhaust the sympathetic nervous system by migrations to the bath-room or toilet as a result of purges, and during the epidemic it was a source of frequent comment that many patients fainted on leaving their beds. Several patients were brought into the Willard Parker with scalp wounds sustained in this way, and in one the question of skull fracture was seriously discussed. These patients have poisoned vascular nerves and a greater mass of blood must be

pumped through the body, and this is best accomplished in the prone position. Even without special nursing, these patients should be provided with urinals and bedpans should be brought to them.

So much for the general handling of these patients. They should be kept in bed, they should not be purged or persuaded that the drinking of much water will rid them of their poisons.

Certain symptoms require special attention.

Headache is best relieved by relieving the congestion through the use of adrenalin dropped into the nose, or by a 4 per cent. antipyrin spray. Adrenalin is preferable because it is absorbed from the mucous membrane and acts as a stimulant. At the Willard Parker, 3 minims of adrenalin chlorid 1 : 1000 are dropped into each nostril, the head being sharply extended over the edge of the bed, and 3 minims placed under the tongue every three hours. This is called the adrenalin treatment. That adrenalin is useful in this way we have ample evidence in the comfort which it gives these patients, and in the improvement in their general condition. If further evidence of absorption were needed I might narrate the case of a diabetic whose sugar tolerance was correctly balanced and in whom 10 drops of adrenalin given under the tongue produced glycosuria.

We have rarely found it necessary to use aspirin, though occasionally 5 grains has seemed to give prompt relief from headache. Occasionally it has been necessary to irrigate the nose. The use of codein or morphin is not indicated for headache alone.

Coughing is another troublesome symptom. This may be due to congestion of the pharynx or even an edema of the uvula. In some cases a spray of 1 per cent. benzyl-alcohol emulsion, which we have extensively employed, both anesthetizes the pharynx and seems to have a distinctly healing action on the mucous membrane. The irritation may be further down the respiratory tract. At times there is subglottic swelling, and even edema and redness of the cords, associated with hoarseness. Sometimes the irritation is in the bronchi. Such cases are best relieved by morphin, or by counterirritation with flaxseed poultices or mustard paste applications, or by drugs which dilate

the bronchi, such as hyoscyamus, 10 minims of the tincture. Sometimes there is a pleurisy. Such cases should be relieved by strapping with adhesive plaster so as to fix the border of the ribs.

Opiates should not be used to the point of abolishing the cough reflex, but the cough should be controlled to the extent that it is only productive. The amount of sputum can be very much reduced by limiting the fluid intake, but this should not be carried so far as to permit the sputum to become too tenacious. If this should happen, bicarbonate of soda by mouth is a useful remedy. Anyone who has seen thro' a bronchoscope a mass of sputum thrown from one bronchus to another must realize that coughing itself spreads the infection in the lung and should, therefore, be controlled. Besides, coughing puts a violent strain upon the circulation in the chest.

The usual irritant expectorants should not be employed. There is no reason for giving ammonium chlorid or other expectorants, such as squill, as a routine. The mucous membranes are already swollen and irritated. Squill, which is present in the ordinary Stokes' expectorant, stimulates the kidneys to excrete water; this is unnecessary if the total fluid intake has been restricted to proper limits. The cough, in the chest cases, is the result of inflammation of the tracheobronchial mucous membrane. Swelling and congestion with subsequent desiccation and exfoliation of the mucous membrane is the pathologic process. For several days the cough is tight; then it becomes loose and productive, and finally disappears even if no drugs are employed, provided the fluid intake has been regulated.

A distressing symptom associated with the cough is pain or tightness in the chest. This may be due to the congestion of the bronchi or to the dilatation of the vessels in the lung. When there is pain, there is usually hyperalgesia, commonly located in the sixth to the eighth dorsal segments or posterior maxima. If the eighth dorsal segment is involved the emphysema reflex may be liberated. If the pain is associated with hyperalgesia, a counterirritant, such as a mustard pack, or cupping, may be employed. Codein or morphin should be employed in these cases early, so as to prevent, if possible, the occurrence of a marked

emphysema. The cases with pleurisy may be relieved by strapping. In one such case where the strapping was ineffectual artificial pneumothorax was induced with prompt relief of pain, immediate fall of temperature, and convalescence.

Dyspnea may be a very trying symptom and may be due to obstruction in the upper air-passages. In some cases tubage of the larynx has been successfully instituted, as recommended by Henry L. Lynah. It is important in these cases to inspect the larynx by the direct vision method of Dr. Lynah lest the obstruction be mistaken for diphtheria. The association, however, of emphysema with a croupy cough and a clear voice are very suggestive of influenzal subglottic involvement.

At times the dyspnea is due to the acute pulmonary emphysema. This may be relieved by counterirritation to the lower portion of the chest, by morphin, and by adrenalin hypodermically administered; in several cases the dyspnea has been relieved by the reduction of increased negative pressure through the performance of a partial artificial pneumothorax.

Very rarely spontaneous pneumothorax is a source of embarrassment if the pressure becomes too high. In these cases the intrathoracic pressure may be reduced by the insertion of a needle.

The most oppressive dyspnea of excessive secretion into the lungs should be anticipated and avoided by the limitation of the fluid ingested. The dyspnea of circulatory weakness must be met by appropriate stimulation.

Occasionally hemoptysis occurs. At times the hemorrhage is massive. In these cases the congestion in the lungs must be reduced by limiting fluids.

Stimulation.—So much misunderstanding exists regarding what is suitable stimulation that it seems worth while to restate the problem of stimulation from my own point of view.

What is the purpose of stimulation? To answer this question requires a statement of those conditions which it is sought to maintain in the circulation, namely, an adequate perfusion of tissue with healthy blood. The circulation may fail by reason of failure of the heart, but this is by no means the most important

point of weakness. In an experience extending, during this epidemic, to over 500 pneumonias I have seen only 2 cases in which death was due primarily to cardiac disease. In these cases there was a disturbance of the heart mechanism. The heart pumps powerfully for a long time after the circulation is hopelessly inadequate, so that we must seek the defect elsewhere than in the heart. If that is the case, what is it we do when we say we stimulate the heart? The problem may be restated from the viewpoint of colloid chemistry. We seek to make a colloid mechanism continue to work adequately. The studies of MacDonald and Burridge on the heart muscle contractions in the presence of various so-called cardiac stimulants are of very great importance in this connection. The contraction of muscle is a colloid phenomenon, which may be expressed as a change in dispersity of the colloid particles. During contraction the colloid aggregates increase; in relaxation they are more dispersed. It has been shown that calcium salts are necessary to contraction, while sodium salts are essential to relaxation. All the so-called cardiac stimulants have been experimentally shown by Burridge to have the property of increasing the utilization of lime by the heart muscle. This is not by any means the same as increasing the amount of lime to be used.

The importance of posture must be borne in mind in handling these cases. Colloidal phenomena are surface phenomena; therefore, increase in the surface area of the heart muscle, of dilatation of the heart, is favorable for heart action, as has been shown by Starling in his Linacre Lecture on the Law of the Heart. It is not only good muscular action on the part of the heart muscle, however, which must be considered in maintaining the circulation. The circulation may fail in spite of strong cardiac contractions, and this may be induced either by actual reduction of the blood mass or by reason of the blood becoming pooled in the body. In extensive areas of inflammation of the lung a large volume of blood may be collected, much larger because of the negative pressure in the chest than in inflammatory areas elsewhere in the body. The blood may not only pool in the chest; it may pool in capillary beds elsewhere in the body, or in the great

veins of the abdomen. This pooling may be produced as a direct action of a toxin on the capillaries or on the autonomic nervous system, or by failure of the autonomic nervous system in consequence of its impairment or exhaustion.

Morphin.—What can we do to maintain the circulation in the presence of the condition outlined above? Probably, in the sense used above, the most important stimulant is morphin. It has a selective action upon the nervous system which biologically and colloidally may be considered a glorified muscle. Many of the phenomena of stimulation and relaxation in muscle are paralleled in the excitation of nerves. Morphin probably increases the utilization of lime by the nerves and assists in the calcification of the synapse. By this action it delays the transmission of impulses through the central nervous system, and in this way prevents the exhaustion of the vasomotor or respiratory centers in response to the painful stimuli from the lungs. It procures sleep. Patients who cannot be made to sleep, die. A $\frac{1}{4}$-grain of morphin with $\frac{1}{100}$ grain of atropin, repeated if necessary on successive nights, has frequently changed the prognosis of desperately ill cases.

Digitalis increases the utilization of lime by the colloids of the heart. I have already stated my reasons for believing that lime metabolism is disturbed in influenza; 15 minims of a good tincture of digitalis three times a day for several days at a time proves a useful stimulation.

Adrenalin acts like other stimulants by increasing the utilization of lime. This effect is exerted not only on the capillaries of the skin and the lungs, but there is also an effect on the heart. Patterson has shown that the output of blood from the heart is increased by adrenalin, especially in the presence of carbon dioxid poisoning. The adrenalin may be given either through the respiratory or oral mucous membranes, or may be injected subcutaneously, 3 to 5 minims are instilled into each nostril and placed under the tongue every three hours; 15 minims may be given every hour or two, if necessary, by hypodermic.

Pituitrin is the drug which we have found most useful. This we have given in $\frac{1}{2}$ c.c. of the surgical preparation every six hours

or oftener hypodermically. The effect seems to be manifold. The most important result is an increase in the blood-pressure. This is probably due to the general action of the drug on all muscle tissue, increasing the strength of contraction by increasing the utilization of lime. This action seems to be on the capillaries as well as upon the heart and other viscera. Obstetricians have long recognized, sometimes to their sorrow, this tonic action on the uterus.

We have not reserved the use of pituitrin for marked tympanites, for when tympanites develops the nerve centers have been badly damaged. The drug diminishes the output of urine and increases retention of products which may increase the viscosity of the blood. In one case it caused anuria lasting eighteen hours without permanent detriment to the patient, who recovered from a three-lobe involvement.

We have not considered pregnancy a contraindication to the use of pituitrin. Twice we have given it to pregnant women in their eighth month without inducing labor. In one patient in whom the circulation seemed about to fail, 1 c.c. of pituitrin injected hypodermically caused a tonic contraction of the uterus and such a marked improvement in the circulation that no further treatment was required.

We were led to adopt the six-hour interval of dosage by our observations in diabetes insipidus, where we noted that the effect of the drug upon the specific gravity of the urine lasted six hours at least.

Alcohol exerts its stimulating action, as Burridge has shown, by increasing the utilization of lime by the muscle colloids just as adrenalin and pituitrin do.

Other Agents.—*Caffein* we have not used because of its irritation of the nervous system, nor have we used camphor, because of its irritating effect upon the subcutaneous tissues. Patients whose nervous system is excited by reason of oxygen deprivation, or exhausted by reason of painful stimuli, should be given morphin by preference. Strychnin in ordinary dosage increases the utilization of lime, but the frequent repetition of hypodermic injections does not raise the blood-pressure, as was

shown by Herrick and, therefore, it is useless to give it for this purpose.

We have rarely sought to restore blood volume by saline infusion, and then unsuccessfully, but we have relied upon the contraction of the circulatory bed induced by the drugs mentioned separately, or we have sought to drive the blood from the lungs by decreasing the negative pressure, either by partial artificial pneumothorax or by posture. The recumbent posture which is chosen by most patients increases the cardiac content 20 per cent., dilating the heart, and thus favoring powerful muscular contraction. Sometimes, however, and I have found it an evil omen, patients rise from bed. This seems to be an unconscious effort to diminish the thoracic content and give blood to the general circulation. One of my worst cases was carried through successfully with the aid of a back-rest. It has seemed to me that the marked circulatory prostration following influenza is due in part to the diminution in blood mass as the result of colloid shrinking which goes *pari passu* with body emaciation, and which is restored slowly with improved nutrition. It must not be forgotten that small areas of infection may continue in the lung or sinuses of the head and require diagnostic ability and *x*-ray assistance for their location. One patient continued weak and miserable for five weeks, when he suddenly collapsed and developed a chill and rise of temperature. Several days later a diagnosable interlobar empyema revealed itself. This man had been frequently examined for the source of his absorption without success.

In conclusion, the whole subject may be summed up by the statement that the phenomena of influenza seem to be the result of profound changes in the swelling state of the colloids of the body in response to an irritant, and from this conception we may build up the clinical picture and deduce the therapeutic indications.

CONTRIBUTION BY DR. WILLIAM H. SHELDON

CORNELL UNIVERSITY MEDICAL COLLEGE

THE HOSPITAL AS A HEALTH UNIT

Criticism of Prevailing Methods in Management of Outpatient Departments of Hospitals. Districting Large Communities of Value in the Prophylaxis and Cure of Disease in its Early Stages. Importance of Functional Re-education. Value of Social Service Department. Necessity for the Study of Practical Problems in Medicine.

IT has become increasingly obvious as the result of the Great War that closer relations must be established between the practitioners of medicine and the general public. The appalling number of men throughout the country shown by the draft examinations to be physically deficient has driven home both to the medical profession and the public the necessity for a closer co-operation and a more general dissemination of the knowledge of both medical and social factors which tend to prevent disease.

There is a wide-spread sense of social obligation today and a more comprehensive idea of the value of individual life than has ever existed before. The apparent callousness of past times is slowly but surely giving way to a desire to ameliorate certain social and medical conditions which have only been touched upon in the past. Therefore, not only is the medical man expected to diffuse his knowledge in a practical way to the public, but he must also call upon the help of the social workers and others who have the power of assisting him in the effort to bring about the general betterment of mankind.

It would seem that the natural unit for this work would be the hospital. But the hospital up to the present has been almost

entirely given over to the purely medical and surgical treatment of the very sick, with little or no attention paid to the prevention of disease. Such factors as those of occupation, environment, etc., have received scant attention, and the educational passibilities of the hospital with relation to the public have been largely neglected.

The most practical way of making the hospital the important educational center it should be is to district the cities so that there will be one hospital to a given district, and arrangements made that no person applying for medical aid be allowed to go to any hospital outside of that district. The advantage of this method of districting is so obvious that it is surprising that it has not been brought about in the past, though it has been very often advocated.

One of the chief reasons why it has not been done is through lack of understanding on the part of the hospital boards of trustees, the members of which are too often chosen because of their social and political importance and wealth rather than for their keen interest in and knowledge of questions relating to the public health. Moreover, the objection has been made that by so districting the cities there would be an uneven distribution of clinical material for pre- or postgraduate instruction. Anyone who has had experience in clinical teaching can easily combat this argument. It is not a small number of patients which produces a lack of clinical material, but insufficiently thorough methods of examination to determine accurate diagnoses which have been responsible for this criticism. Too often clinicians prefer to pass over a vast amount of material and pick out the obviously sick rather than be more careful in their examination of every patient in order to find cases of disease in its incipiency.

The competition between hospitals has also been a great factor in preventing this districting. Boards of trustees have been prone to point with pride to the large number of patients treated at low cost per patient rather than to records showing a smaller number of patients treated, but with a high percentage of relief and cure.

We should not look so much at the question of the large num-

ber of patients treated as to the welfare of the individual. Therefore, every individual who applies for treatment at the hospital must be carefully examined and his condition diagnosed by all known methods in order to insure proper treatment. That this is done in a large number of in-patient departments in the hospitals is, of course, true, but owing to the slipshod and careless methods of the out-patient departments it is only the obviously sick that, in a large proportion of cases, ever gain proper care. Owing to the pernicious idea that has existed and still exists in relation to the *numbers* of patients treated, the out-patient departments have been exploited in a most disastrous manner, and have been more and more neglected, until at the present time conditions are such that it is difficult to get the graduate of the modern medical school and hospital to work in such a department. For in such a dispensary the doctor is a sort of clerk who sits at a desk and writes prescriptions. He has little time to utilize methods of diagnosis even though they are supplied to him, which is seldom. A large number of the patients seen in this way naturally form a very poor opinion of the practice of medicine, and this growing feeling on the part of the public is of very serious import.

If we are to get the necessary clinical material out of a smaller number of patients, the cost per patient is obviously much greater. But this objection may be obviated by the fact that the economic waste of the present system is tremendous. Why such a large percentage of hospital funds should be spent upon in-patients, quite a proportion of whom are hopelessly ill, and so small a part of the funds, if any at all (many hospitals actually making something from out-patient departments), appropriated to the out-patient department, where a large number of the patients are in such condition that their disease may be either arrested in its incipiency or cured, is one of the mysteries of our medical times. The prophylaxis and cure of disease in its early stages in a large number of persons is of greater economic importance and far greater benefit to the community than the study and relief of a comparatively small number in an advanced state of illness.

If we have the cities districted, as suggested, all sorts of possibilities for good work will be presented. In the first place, such a districting would soon change the point of view of the managers of hospitals. More perfect equipment of the out-patient department would have to be installed, more modern methods of diagnosis adopted, and an adequate staff of doctors provided.

In organizing the staff of the up-to-date dispensary it is essential that the chief of the service should be selected not only because of his known ability in his specialty but also that he should be able as a teacher to instruct his assistants. This is of the greatest importance. Men working in clinics do so primarily to gain knowledge, and frequently, because of the lack of diagnostic facilities in the clinic and insufficiency of time and the inability of the chief to instruct them, they get discouraged and give up the work. Another important point is that every man should receive credit for good work done and his efforts should not result in his work being exploited for the benefit of the chief. As he deserves it, he should receive advancement and opportunities. This also applies in the case of surgical clinics where, as things are organized at present, the chief of the service frequently takes all the interesting operations, and under these circumstances his assistants have little opportunity to gain confidence and operative ability of their own. Taking it for granted that there shall be established an out-patient department on strictly modern lines, comparable to the service within the hospital, there will be almost unlimited opportunities for the extension of work in a given district.

One of the most important considerations of the present day in connection with the welfare of the community is to have every individual thoroughly examined and their difficulties and weaknesses pointed out. This could be accomplished by a sufficient number of well-equipped out-patient clinics. I believe that with a little advertising such institutions would receive the cordial support of the population of each district, were it understood that not only the sick but the well who wished a physical examination could apply and receive adequate attention. Could

we get them so to apply, our facilities for improving public health would be enormous. No one who has worked in out-patient departments for many years can doubt the truth of this assertion. Those of us who aided in conducting the draft and who have been in dispensaries for a number of years have observed an enormous number of defects in individuals which will ultimately become a menace to their health, and possibly their lives, which could be easily rectified had we adequate control of the patients and facilities for correction.

As an example, take the question of the teeth. Roughly, I should say, there is not one person in a hundred among working men and women who does not need dental attention. The condition of the mouths of many is to be observed only with amazement. Pyorrhea in its most advanced stages, obviously abscessed teeth, dental caries, and other of the most gross lesions exist, and at the present time we have few facilities for their correction. Each out-patient department of the city should have an adequate dental department, and when these conditions are found the patient could immediately be referred to this department for correction.

For an example in another field, take neglected and badly treated fractures and injuries, as well as those treated by the most modern methods of ordinary surgery. The number of cripples who have lost function through lack of attention to functional re-education is amazing. I have talked to a large number of corporation physicians, and they all tell the same story: No matter where they send the patient, even to the most approved scientific hospitals, he gets surgical treatment, but not functional restoration. Now in the treatment of soldiers, both abroad and in this country, it has been shown that there are possibilities in functional restoration which were heretofore undreamed of. Unfortunately in America we have only one civil institution as yet for functional re-education, the Clinic for Functional Re-Education in New York City. The equipment for this particular work includes apparatus for hydrotherapy, electrotherapy, thermotherapy, and mechanotherapy. It is a well-known fact that physicians are not practising what they

preach in connection with these methods of therapeutics, but I think there are few who do not thoroughly believe in them. Yet how many hospitals have more than two such departments for this purpose at the most? and yet it has been proved that the use of all these methods is absolutely necessary for the correction of deformities. They are applicable not only to the correction of deformities but also to a large number of patients with nervous and internal disorders. In fact, in a very large group of cases the principal therapeutic reliance must be placed upon these various methods of physiotherapy.

We may also point out what is obvious, that they are of enormous advantage in the treatment of a large variety of medical cases. The cost of installing the appliances necessary for this treatment is very great, but the number of cases referred by casualty insurance companies is so large that such a department, with their co-operation, would be largely self-supporting. Manufacturers are becoming increasingly aware of the fact that they are unable to get restoration of function for their injured employees, and they are becoming anxious to see that such means are provided. Without doubt their cordial support and co-operation would be given to such a department, properly run, in the hospital.

There is a great need in connection with every hospital for the establishment of a gymnasium. Present methods of handling the subject of scientific exercise are much to be deplored. Men who are put into the gymnasia do largely as they please. Some overexercise, a few underexercise, and the patient is liable to overdevelop certain parts of his body to the detriment of other parts. Very little stress is laid upon the development of chest and abdominal muscles, which, after all, is most needed to insure good health. In gymnasiums the correction of deformities is largely neglected. During the winter of 1917–18, at Cornell Medical College, we conducted a class for rejected men, navy and marine. These men were all unfit, underdeveloped, or had some cardiac functional conditions. Many of these men had been attending Y. M. C. A. and other gymnasia where they had practically no oversight and had become utterly discouraged from ob-

taining no results. By means of our system of exercises and directions in hygiene and diet a large number overcame their defects, volunteered again, and were accepted. In these classes it was not uncommon for the men to gain from 1 to 3 pounds a week for a number of weeks in the correction of their physical deficiencies, without the use of any apparatus, simply by exercises devoted to the improvement of their specific defect. This small experiment was sufficient to show the economic gain that could be derived from such methods. (See preliminary report, New York Medical Journal, October 19, 1918, p. 703.)

There are a large number of our hospital patients whom we could refer to a gymnasium with the expectation of ridding them of many of the sources of their ill health. I feel sure that such work could be undertaken with the proper oversight and point of view in mind, but at the present time I know of no public institution in New York City to which a patient can be referred and obtain attention and proper direction for any specific condition. Such a gymnasium need not have elaborate equipment. A well-aired room, a few simple pieces of apparatus and mats are all that is required, and this could be run at a very moderate cost. The correction of one class of patients alone would be adequate incentive for the establishment of such a gymnasium. Patients with low-placed stomachs and colons have shown brilliant results from such gymnastic treatment, and yet at the present time our large gastric clinic at Cornell has been unable to find a single public institution where we can refer our patients for proper attention and results. Our knowledge that such results can be obtained is founded upon our experience, as we have had private instructors take charge of the correction of our dispensary patients and produce the given results. Moreover, all doctors know that by referring patients to properly superintended private gymnasia they are able to obtain the desired results. The use of exercises in cardiac cases also has become of increasing value. During the war thousands of patients with certain cardiac disturbances were treated by such methods by the governments of England, France, and the United States, with gratifying results.

If we had hospital districts in the city with adequately equipped out-patient departments the educational possibilities, in addition to the correction of obvious defects, would be enormous; lectures and talks could be given on various subjects of hygiene; the question of personal health could be emphasized; leaflets with information as to the most approved methods of caring for the general health could be distributed; lectures on the prevention of infectious disease would be of value; industrial hygiene would be of importance; and the public could be brought to realize the significance in the relation of industry to public health.

The hours of work which are so much discussed at the present time have largely been left to the careless and indiscriminate decision of labor leaders compromising with the desire of the manufacturer to get the longest number of hours possible from the men. The hours of work are really a medical problem, inasmuch as the health and welfare of the individual are the ultimate reasons for the duration of work, and yet at the present time the medical profession has had very little to say on this all-important subject, largely through lack of realization of how much the health of the individual depends upon the kind of work he does or the number of hours in which he does it. Large corporations are becoming increasingly aware of the desirability of medical opinions on these subjects, and many concerns have a medical staff organized to consider this problem among others. It is interesting to note that with somewhat reduced hours and the same pay many concerns are finding that there is actually an increase in the amount of work accomplished.

It seems as though through a thorough medical study of this subject many of the inequalities and injustices in the demands of both labor and capital could be settled. It is obvious that if an individual works for sufficiently long hours to injure his health the employer is not getting the best benefit from his services. If this could be pointed out by a thorough medical study, many difficulties would be smoothed out. On the other hand, too short hours of work, while theoretically not injuring the health of the individual, in actual practice may do so; it largely depends upon

what the individual is going to do with his hours of leisure, and if these are unduly long the time spent in pool-rooms, bars, saloons, and other undesirable places would actually be worse for the health of the individual than if he were at work.

The question of food for the worker could be gone into extensively. Modern medicine contains many phases of scientific knowledge as to the desirability, cost, and value of various articles of food, and yet the general public, in spite of the educational campaign which has been conducted during the war, seems to be largely ignorant of the facts which have become common knowledge in medicine.

Information concerning these matters of health and hygiene could be conveyed to visitors to the clinics by means of printed leaflets. Cornell University Medical College, I believe, was almost the pioneer in the printing of slips for clinic patients. Some nine or ten years ago, with the cordial support of W. Gilman Thompson, I wrote a series of slips[1] which we have been distributing ever since. These include instructions for patients with nephritis, heart disease, diabetes, constipation, gastric ulcer, chronic gastritis, hypochlorhydria, lead-poisoning, chronic joint disease, and chronic bronchitis. The slips give the patient definite rules to follow as to his daily routine, food and habits, and the precautions necessary for him to observe to combat his disease. It is explained why it is necessary for him to follow these rules and the benefit that will accrue to him if he does so. There is a detailed diet list for each group of cases. There is also a leaflet on the general care of health, and a pamphlet on diet, with balanced menus and rules for cooking.

To indicate the prevailing interest in this subject, we have been asked by scores of corporations, such as insurance companies, colleges, and hospitals throughout the country, for several hundreds of sheets of these printed slips for distribution, and have even had requests from medical schools in foreign countries for such slips, and permission to translate them. We have been increasingly impressed with the value of such slips. Not only is good done to the patient, but very often the health of the whole

[1] See Printed Slips for Clinic Patients, Medical Record.

family is improved by his newly acquired knowledge of hygienic matters. An extensive campaign of printed slips in any district would surely be of enormous value.

In order to accomplish all that is desired in the scheme which is here outlined an extensive department of social service would be necessary. Medicine in the past has too often stood away from the practical problems, as I think I have indicated, and it is generally accepted now that the health of the individual is more than a matter of germs or the ordinary considerations which we take up in medicine. It is the outcome of the combination of all the circumstances which surround the individual—the place, method of living, wages, working place, the number of children in the family, etc.—all those elements which we know enter into the problem of the individual. This becomes increasingly important at the present time during a stage of economic unrest. In a hospital district such as we propose it would be necessary to have the social service workers investigate not only the conditions which we have mentioned but also help in the problem of education.

For example, if a man comes to the out-patient department and has bad teeth, it should be the duty of the social service to follow up that man until his mouth condition is cured. If a man is suffering from psychasthenia, it should be the duty of the social service to investigate his home to see whether his surroundings are compatible with his mental health. Too often we try to cure by medicine instead of curing social conditions the difficulties of which are really overwhelming the individual. Perhaps it may be a low wage with a large number of children, or insufficient food, or little prospect for the future.

I believe that an adequate social service could do much toward remedying the problem of infectious diseases. While this is a function essentially of the boards of health, their data is so lacking in correlation as to districts, and conditions of living are so inadequately followed up that it is far from satisfactory, and one cannot form any very accurate deductions from their statistics. If all the sick poor were from a certain district or if most of them were reporting to a given hospital, it would be quite

easy for a social service department to gather accurate statistics as to the prevalence of certain diseases in certain sections, just as the tuberculosis district clinics have been of enormous value in the collection of such evidence. If in a certain tenement there are a number of cases of typhoid, that tenement could be investigated as to the presence of carriers or other sources of infection, and future cases eliminated. We can cite example after example in this line. Certain blocks in a district would be found to be especially unhealthful. The social service could find out the elements which caused this. Unsanitary conditions of tenements, disobedience to tenement laws, and other causes of misery could be pointed out, and reform made easier.

Moreover, there is no reason why such a social service could not be extended, or even the question of employment considered. Every section of all great cities has cripples and other handicapped individuals who are thoroughly discouraged and need help to obtain work that is suitable for them. That such an idea as this is capable of practical application is being shown at the Clinic for Functional Re-Education, where placement is a branch of social service. At this clinic the possibilities of the individual are carefully investigated, his physical handicaps noted, and he is brought into contact with various agencies distributed throughout this city and other cities, and encouraged in every possible way to adopt some employment which is suitable to him. Not only that, but connected with the social service there is a board of advisors made up of men prominent in various lines of endeavor, who are willing to take their time to consult with these individuals and advise them as to the opportunities and advancement in their special line of work.

The social service as related to occupational conditions has an importance which can hardly be exaggerated. In the case of chronic cardiac disease there is a great need of putting these people in proper vocations. As it is, a large number of cardiac patients either become chronic invalids or do work that is unsuited to their condition. It is a very pitiful condition of affairs when a man has to pursue an industry which in the course of six months to several years will surely kill him, and where the

facilities for his readjustment are so slight. By co-operating with such institutions as now exist, and should exist were our system established, institutions such as the Bureau of the Handicapped, more extensive study could be made of cardiac patients in order to understand better what positions in industry they are fitted to fill and those they are not fitted to fill.

The same reasoning applies to tubercular patients, but that subject is fairly well taken care of by present organizations and board of health clinics.

By the investigation of patients coming to hospitals evidence is soon found of the relation of industry to disease, and by a large number of such observations and investigations classifications can be made as to how the individual reacts to certain types of work. An interesting example of this was demonstrated a few years ago. A certain street railway, with the kindest intentions, supplied the motormen with stools, but the stools were all of the same height. A social worker observed that in the Cornell Clinic there were a number of men suffering from sciatica who were employed by this company. On investigation it was found that owing to the standard stool the taller individuals got a continuous pressure on the sciatic nerve through ringing their gong with the right foot, which brought on a neuralgia. The attention of the company was called to the defect and stools of varying height were supplied. In this way probably hundreds of cases of disability were avoided by the company and considerable misery escaped by a number of motormen.

Cases of lead-poisoning came to our attention in a dozen individuals, foreigners who could not speak English, who were found to come from a certain factory. Investigation showed that in this factory, which was run largely by foreign labor, warnings as to the dangers in the manufacture of white lead were only printed in English, and therefore, while the few English employees were not acquiring cases of lead-poisoning, a large number of the foreigners were. When this was pointed out to the manufacturer the head of the factory had the warnings printed in various languages, and the number of cases of lead-poisoning was enormously diminished.

Cases have been discovered by the social service and called to our attention where workers in various trades, through lack of knowledge on their and the manufacturer's part, were seriously affected by bronchitis through respiration of dust. By instructing these individuals in how to guard against this by wearing face-masks the dangers were largely done away with.

There is no reason why such a social service could not go into the problem of occupational therapy. A large number of people coming to hospitals are not physically fitted for their regular work. These could be trained in basket making, rug making, typewriting, bookkeeping, and other occupations suited to their handicaps. At the Clinic for Functional Re-Education the Social Service Department has worked out an entirely practical solution of the difficulties of many men.

Through such a social service as is proposed it would be possible to help people to find recreation, for, as is well known, healthful recreation is one of the solutions of many medical and social problems. Information could be given as to free lectures, free dances, moving pictures, etc., and the patients encouraged to go to the museums and other public places of interest, and in this way be aided in getting normal recreation. It would be a great advantage to bring the patients needing relaxation into contact with the various forms of wholesome pleasure which exist, for often they are unaware of even the greater organizations of our country, such as the Y. M. C. A., Knights of Columbus, and others who are working for the betterment and happiness of the individual.

There seems to be every reason why there should be closer co-operation between the public schools and such a district hospital as is here outlined. The hospital physicians could be examining physicians of the schools, and as defects are discovered in the students, they could be referred to the hospital where there would be adequate facilities for correcting these defects, and not, as is so often the case now, defects diagnosed and yet not corrected. Does it not seem that this could be of enormous advantage to the community at large and an economical arrangement of the school and city authorities? This also has the ad-

vantage of removing the school physician from politics, and the fact that the examining physician is subject to the authority of a well-organized hospital would be sufficient indication of his ability and honesty. The city could well afford from the economic standpoint to pay the hospital for such services rendered both as to examination and as to correction of defects.

CLINIC OF DR. A. S. BLUMGARTEN

Lenox Hill Hospital

CASES ILLUSTRATING DIAGNOSTIC PROBLEMS

I. Primary Malignant Tumor of the Lung. II. Cerebrospinal Syphilis. III. Three Cases Illustrating Problems in Nephritis: (*a*) A Problem in Diagnosis. (*b*) Problem in Treatment. (*c*) A Problem in Prognosis and the Effect of Decapsulation. IV. Two Cases Illustrating the Diagnosis of Aortic Syphilis: (*a*) Early Aortic Syphilis. (*b*) Aneurysm of the Arch of the Aorta.

I. PRIMARY MALIGNANT TUMOR OF THE LUNG

R. H., a machinist, thirty-seven years of age, married, was admitted to the Lenox Hill Hospital complaining of sore throat, pain in the left side of the chest, slight hoarseness, and loss in weight.

The illness began two months before admission with an attack of bronchitis while he was in the mountains. He lost 5 pounds at that time, and after his return he continued to lose in weight until at the time of admission he had lost 35 pounds. For five months before admission he had persistent pain in the left side of the chest, and for two weeks he had a slight hoarseness and a sore throat. At times he became nauseated after eating, and this was often accompanied by headache.

He had diphtheria at the age of thirty-five. His appetite is poor, he drinks 1 pint of beer a day, and smokes about three pipes of tobacco and an occasional cigar daily. He denies lues. One of his brothers died of tuberculosis some years ago.

The history is that of a primary pulmonary condition with a subsequent involvement of the larynx. There is no clue in the

history that might be of diagnostic value other than the loss of weight and a very remote family history of pulmonary tuberculosis. Indeed, the patient was sent into the hospital from the dispensary with a diagnosis of pulmonary tuberculosis.

Physical examination shows a middle-aged man, quite anemic, and suffering only from hoarseness which has grown progressively worse while he has been under observation. The chest is normal

Fig. 222.—Roentgenogram of chest of R. H., showing mediastinal mass in case of primary malignant lung tumor.

in shape. There is an area of dulness over the mediastinum about twice the normal width, extending from the suprasternal notch to the area of cardiac dulness in the anterior left chest. Here there are signs of a large amount of fluid, which on repeated puncture proved to be serosanguineous in character. There are signs of a small amount of fluid at the base of the right chest posteriorly (Figs. 222–224).

Examination of the abdomen is negative. Examination of the extremities shows no evidence of any lesion.

The urine examination was negative. The sputum has been examined a number of times, but no tubercle bacilli were found. The blood-pressure was 110 systolic and 80 diastolic. The Wassermann examination of the blood was negative. The Wassermann examination done again ten days after a provocative sal-

Fig. 223.—Roentgenogram of chest of R. H., showing increase in size of mediastinal mass while patient was under observation and mass in lung. Case of primary malignant tumor of lung.

varsan injection was also negative. The Wassermann test of the spinal fluid was negative. The blood count shows evidence of secondary anemia with 75 per cent. of hemoglobin. About five days after admission 10 c.c. of a serosanguineous fluid was removed from the left chest and carefully examined for evidences of tumor cells, but none were found. On culture, this fluid was sterile.

The only evidence, therefore, of a pathologic lesion in this case is in the chest.

The presence of a serosanguineous pleural fluid at once indicated the necessity of an *x*-ray examination of the chest, and the roentgenograms reveal the presence of a mediastinal mass involving the entire mediastinum from the suprasternal notch to the cardiac shadow. The mass itself is irregular in outline and did not pulsate on several fluoroscopic examinations.

Fig. 224.—Roentgenogram of chest of R. H., showing mediastinal mass and definite mass in lung. Case of primary malignant tumor of lung.

Examination of the larynx showed a paralysis of the left recurrent laryngeal nerve, and repeated examinations of the larynx showed that this paralysis became complete while the patient was under observation.

Gradually we noticed that an inequality of the pupils developed, the left being smaller than the right. (This may have been due either to pressure with almost complete paralysis of

the left sympathetic nerve, or to pressure with irritation of the right.) Both pupils show a diminution in reaction to both light and accommodation.

The case, therefore, presents the possibility of the following lesions, with their inherent difficulties in differential diagnosis: 1, Mediastinal tumor; 2, aneurysm of the arch of the aorta; 3, lung tumor.

The occurrence of a recurrent laryngeal paralysis would seem to point to a mediastinal lesion. The pulmonary symptoms, however, were present for a long time before the occurrence of hoarseness, the symptom which actually brought the patient to the hospital. Furthermore, a large amount of serosanguineous fluid is present in the left chest which precludes the determination of a mass in the left lung by physical examination. In spite of the fact that the presence of a mass cannot be shown in the left lung even by the *x*-ray examination, the occurrence of persistent pulmonary symptoms on the left side for such a long time, together with the presence of a large amount of serosanguineous fluid in the left chest, would still suggest a lesion in the left lung. The involvement in the left recurrent laryngeal and sympathetic nerves very late in the course of the disease increases the probability of a lung tumor as the most logical diagnosis. If it is a lung tumor, it is probably malignant, and we can explain the finding of the mediastinal mass as a secondary metastasis.

We may exclude the presence of an aneurysm by the absence of the physical signs of an aneurysm, by the lack of pulsation in the fluoroscopic examinations of the mediastinal mass, by the absence of a syphilitic history, and by the negative Wassermann test in both blood and spinal fluid. We must bear in mind, however, that an aneurysm in the arch of the aorta is the most common mediastinal tumor encountered.

About three weeks after admission we first felt in the left supraclavicular space a rather flattened nodular mass about the size of a walnut which seemed to be firmly adherent to the apex of the lung. This was probably a metastatic supraclavicular carcinomatous lymph-node.

A few days later a bronchoscopic examination was done by

Dr. Felix Cohn, who found the following lesion: In the region of the trachea about the bifurcation but above the larynx was seen a stenosis. The lumen was elliptical, the long diameter being from the left anteriorly to the right posteriorly, and it seemed to be due to a right-sided pressure. Its structure was soft, as the bronchoscope easily dilated it and passed it. The lumen was filled with mucus and was in itself quite small, making it very difficult to see the tracheal bifurcation. The vocal cords were apparently involved similarly, as they did not move on respiration.

Although study of the roentgenograms shows the presence of a mediastinal mass with radiations into the hilus of both lungs, and accordingly we could be tempted to diagnose a primary mediastinal tumor with secondary involvement of the lung, this does not correspond to the clinical history of the disease. The clinical course and the presence of a left supraclavicular node would seem to indicate that the case is one of primary lung tumor with secondary involvement of the mediastinum rather than a primary mediastinal tumor with secondary lung involvement. The study of the later *x*-ray pictures, taken several days after the first ones, seems to show a more definite lung involvement on the left side. To correlate this finding with the clinical course, it is probable that the tumor may have originated in the region of the hilus. The history of marked cachexia and the occurrence of metastases and a serosanguineous fluid in the chest all point to the tumor being a malignant one, probably a sarcoma or carcinoma. Such a tumor would be more apt to originate in the region of the hilus rather than near the pleural surface, which is the common site for endotheliomata and which produces cachexia late in the course of the disease.

We should, therefore, consider the case as a primary malignant tumor of the left lung, originating in the region of the hilus and producing metastases in the mediastinum and left supraclavicular node. We cannot say whether it is a sarcoma or a carcinoma, although sarcoma is the more frequent tumor in an individual of the age of this patient.

Note.—Subsequent to the above the patient died about one

month after his admission to the hospital. An autopsy, performed by Dr. G. H. Rohdenburg, showed a neoplasm of the left lung with extension into the mediastinum. The following chest findings were the only important pathologic lesions:

The pleural cavity of the left side was obliterated by dense adhesions to the parietal wall. That of the right side was divided by numerous firm adhesions. On removing the larynx, lungs, and heart *in toto* the following condition was seen: Behind the trachea and almost completely encircling it was an irregular, lobulated, firm mass, yellowish-white in color, which extended anteriorly over the aorta from the supraclavicular notch to the base of the heart. Posteriorly it extended from the level of the clavicular notch to the diaphragm and laterally for a distance of 10 cm. to the left and 5 cm. to the right of the aorta. This mass was a direct continuation of a circular encapsulated mass in the upper posterior portion of the upper lobe of the left lung. The mass in the lung measured 7 cm. in diameter.

On section, the growth showed a striated appearance and a milky juice could be expressed from it. The neoplasm completely encircled and obstructed the lumen of the trachea at the bifurcation.

The right lung showed two small areas of healed tuberculosis at the apex, but was otherwise normal. There were no gross metastases in either lung.

The heart and pericardium were normal.

Microscopic examination of the tumor showed it to consist of cells, in general packed closely together and showing no special arrangement, although there were areas in which the cells were collected into islands or columns or formed the lining of alveolar spaces. The nuclei of the cells were round or ovoid, rich in protoplasm, and filling up the greater part of the cell. Mitotic figures were fairly abundant. The stroma varied in amount, but was relatively scanty. Fibrils separating the individual cells could not be demonstrated.

Anatomic diagnosis: Sarcoma.

II. CEREBROSPINAL SYPHILIS

M. K., a widow, forty-seven years of age, was admitted to the Lenox Hill Hospital complaining of pain in the lower abdomen for the past week which was made worse by eating. The illness began with cramp-like pain in the lower abdomen. The pain did not radiate. She took an emetic a few days before admission, which did not relieve the pain. About this time she had gaseous eructations after eating and a sour taste in the mouth. She had chills at the onset of this illness and again the day before admission. She had not eaten anything for three or four days because of lack of appetite and because food gave her pain. The bowels had not moved for a week, nor did she pass any urine during that time until the day before admission. There was no past history of any definite condition other than an attack of rheumatism eight years ago, at which time her wrists and ankles were swollen, but she was not confined to bed very long. She had a pubiotomy done at childbirth.

Ordinarily, the patient does her own housework. She drinks an occasional cup of coffee and her appetite is usually good. She does not take alcohol in any form. Her bowels move regularly and she urinates about five times daily and twice at night. She sleeps well.

Menstruation began at the age of seventeen and was always regular until the age of twenty-six, when her first and only child was born. Following this birth she had amenorrhea for only eight weeks, when she began to menstruate again very profusely for about two weeks, and this was followed by a foul leukorrhea for some time. Since that time she has never menstruated and there is no history of miscarriage.

The patient's father died of erysipelas at the age of sixty and her mother of dropsy at the age of seventy-two. She has one brother and one sister, both of whom are living and well.

Physical examination shows a small, poorly nourished woman of middle age, but who looks older than she really is. She is of almost dwarf-like stature. There is a slight pigmented eruption about the chest, front and back, and both the skin and mucous membranes show evidence of marked anemia.

There is no evidence of any glandular involvement.

Examination of the head shows no evidence of any lesion until the face is examined, when ptosis of the left eyelid is observed, as well as an external strabismus of the left eye. Both pupils are fixed and there is no reaction to light or accommodation. The nose is apparently normal except for obstructed breathing on the right side. The ears are apparently normal; there is no discharge from the canals nor is there any tenderness in the region of the mastoid. The mucous membrane of the mouth is pale and the tongue is markedly coated with a distinct marginal redness, but there is no evidence of any paralysis. The pharynx is apparently normal. There is no evidence of any lesion of the neck except pigmentation of the skin on the right side.

Examination of the chest shows a marked scoliosis of all the dorsal vertebræ with a deviation of 2 inches to the right. The left side is considerably sunken, with a compensatory prominence to the right. Anteriorly the bony structure of the chest is quite normal and the intercostal grooves are quite marked, though the left side of the chest is much more prominent. The breasts are very small and undeveloped, but show no pathologic lesions.

Examination of the lungs shows only slight dulness over the right scapula, which is probably due to the deformity. The heart is somewhat enlarged, though its shape and position are fairly normal, the apex-beat being felt 1½ inches to the left of the left nipple line. The sounds are regular, of poor muscular quality, and a marked systolic murmur can be heard at the apex, which is transmitted upward and backward toward the axilla.

Examination of the abdomen shows very flabby walls, absence of subcutaneous fat, and a loss of tone in the abdominal muscles. The liver and spleen are not palpable. There is marked tenderness on pressure in the epigastrium and the right upper and lower quadrants of the abdominal wall is hyperesthetic. No masses can be felt. The bladder was distended to the level of the navel. The bladder was catheterized and 675 c.c. of a cloudy fluid were obtained. The ascending colon was quite distended and tender on pressure.

The extremities show only an absence of knee-jerks. There is no edema and no evidence of any lesion. Vaginal and rectal examinations were negative.

Eye examination by Dr. Diem showed an incipient cataract in the left eye and a left ophthalmoplegia *externa* and *interna*. The fundus of the right eye was normal.

Careful examination of the nervous system showed only the following positive findings: 1, Sluggish mentality; 2, left ophthalmoplegia *externa* and *interna*, inequality of the pupils both of which are irregular, the left being wider than the right, an Argyll-Robertson, an external strabismus of the left eye, and a ptosis of the left eye; 3, hyperestheisa of the lower extremities; 4, absence of knee-jerks; 5, paresis of the bladder and colon.

Urine examination on admission gave an alkaline reaction, specific gravity 1021, trace of albumin, 0.3 per cent. sugar, trace of acetone, many leukocytes, a few urate crystals, and many bacteria. Two weeks later, examination of the urine showed it to be very turbid and to contain very many pus-cells and many red blood-cells, including a few small blood-clots.

Examination of the gastric contents showed free acid of 38, total acidity 62, a suggestive lactic acid test, and blood by the guaiac test. Microscopically, a few partly digested starch granules and fat globules could be seen.

Chemical examination of the blood showed a CO_2 combining power of 57 and blood-sugar per cent. 0.076.

Roentgenographic examination of the genito-urinary tract taken five days after admission failed to reveal any calculi in the kidneys or in any part of the urinary tract. Roentgenographic examination of the stomach showed it to be normal in size and with no evidence of ulcer. There was, however, some six-hour retention, which was probably due to spasm. There is also an appearance of spasm at the cardia which is quite marked. Fluoroscopic examination eliminated the possibility of a malignant condition of the lower end of the esophagus and proved it to be a cardiospasm.

Blood examination done about six days after admission showed red blood-cells 3,970,000; white blood-cells 5600, poly-

nuclears 77 per cent., small lymphocytes 14 per cent., mononuclears 5 per cent., transitionals 3 per cent., eosinophils 1 per cent., hemoglobin 75 per cent. The clotting time of the blood was four minutes. The blood-pressure taken five days after admission was systolic 130, diastolic 85. The blood Wassermann done about six days after admission was 4 plus. Twenty days after admission a lumbar puncture was done and 20 c.c. of a clear fluid was withdrawn under considerable pressure. Examination of this fluid showed a cell count of 75, globulin of 3 to 4 plus, and a 10 plus Wassermann. Colloidal gold test done on this fluid was unreliable.

This history in a woman of the age of this patient would give the impression of a gastric or hepatic lesion, probably malignant, or of a renal lesion. From the sudden onset of the symptoms, however, we might possibly suspect a crisis in the course of a nervous condition. The only factor in the history that might be of etiologic value is the fact that at the age of twenty-six, eight weeks after the birth of her child, she developed a persistent uterine discharge, and she has never menstruated since nor has she had any other children. It is possible that at that time or a short time previously a luetic infection might have occurred. The only data with reference to the child born at that time is the fact that he is now twenty-one years of age, and that he voluntarily entered the army and later deserted. (We might possibly consider this a stigma of low mentality.)

On examination we find an old dwarf-like woman who seems to be quite emaciated. Her mentality is decidedly sluggish. Examination of her chest shows only a marked scoliosis with convexity to the right and the signs of a chronically depressed right lung, as well as an old, evidently rheumatic valvular lesion. Examination of her abdomen shows a hyperesthetic abdominal wall, with tenderness on pressure in the right upper and lower quadrants, and evidence of a distended bladder and a distended and tender ascending colon.

Examination of her nervous system shows a decidedly diminished mentality, unequal and irregular pupils, the left being wider than the right, but both giving an Argyll-Robertson reaction.

There is also a ptosis of the lid and external strabismus, as well as cataract in the left eye.

The history in this case is very misleading, giving us no clue to her neurologic condition. It is that of an abdominal condition with an etiologic factor that might be considered a source of a luetic infection. The physical findings, however, seem to point to a lesion in the nervous system involving areas widely separated; namely, the third nerve nucleus in the corpora quadrigemina and the lower lumbar segments of the cord. Because of the marked divergence of the areas involved the lesions are evidently produced by a vascular disturbance, probably an endarteritis.

Since syphilis is the most common cause for such a lesion in a woman of the age of this patient, and since we can determine a probable definite source of infection in the history of the case, this evidence points to a cerebrospinal lues, in which the lesion is an endarteritis involving the vessels of the third nerve nucleus and the lower lumbar segments of the cord. The Wassermann reaction in the blood increases our suspicion as to the nature of the infection, and the Wassermann reaction of the spinal fluid corroborates the syphilitic origin of the condition.

Now that we have determined the case to be one of cerebrospinal lues, let us attempt to determine the nature of the pathologic lesion. There are three possible pathologic processes: 1, Syphilitic basilar meningitis; 2, syphilitic endarteritis of the brain and cord; 3, gummatous infiltration of the brain.

We may eliminate a syphilitic basilar meningitis from the fact that there are no signs of meningitis present; there is no rigidity of the neck; no Kernig's sign; no Babinski; the patient does not complain of headache nor does she vomit. Furthermore, if a syphilitic basilar meningitis were present, other cranial nerves besides the third would be involved; but since the only nerve involved is the third, the lesion in the brain must be in the third nerve nucleus.

A gummatous infiltration may be eliminated from the fact that even the involvement of a small area of brain tissue would give much more extensive signs than those present, nor would

two widely separated lesions of such a character occur simultaneously.

The presence of an endarteritis may be established by the apparent chronicity of the condition, by the evident smallness of the area of nerve tissue involved, by the widely separated areas involved, and by the fact that this is the most common syphilitic lesion of the nervous system in an old person. The evidence pointing to a lesion in the lower lumbar segment of the cord is the hyperesthesia in the lower extremities, the absent knee-jerks, and the evident interference with the lower lumbar reflex arcs, as is shown by the paresis of the bladder and colon.

The symptoms for which the patient was admitted to the hospital, however, were those of an acute abdominal lesion, There was no evidence of any lesion of any of the abdominal viscera until roentgenographic examination was made, which showed spasm of the cardia. From this fact, and the fact that the symptoms occurred suddenly, we might consider the abdominal symptoms as those of a gastric crisis occurring in the course of a cerebrospinal lues.

About eighteen days after admission we could feel a distinct tender mass on pressure over the right hypochondrium, and repeated careful examination of this mass showed that it was probably a kidney. The *x*-ray examination of the genito-urinary tract showed no evidence of stones. From the urinary findings, in addition to the findings on manual examination, we should consider this mass as a pyelonephritis of the right kidney, evidently an ascending infection from a cystitis associated with paresis of the bladder. It is quite probable that the original attack of an acute abdominal lesion for which the patient came to the hospital might have been produced by this kidney lesion.

III. THREE CASES ILLUSTRATING PROBLEMS IN NEPHRITIS

(*a*) **Illustrating a Problem in Diagnosis.**—J. H., a theater clerk, twenty-five years of age, was admitted to the hospital suffering from generalized edema. Eight weeks before admission he noticed that his face, legs, penis, and scrotum had become markedly swollen. The edema did not disappear on lying down.

He also complained of severe headache at times, and had periods when he was quite drowsy, but he had no vomiting and no nausea. The edema of the eyes and face decreased somewhat during the day. He had dyspnea on exertion, but no cough. He had marked polyuria, voiding every two hours during the day and four times at night, and passed about one quart of urine in twenty-four hours. At times the urine was cloudy and he noticed blood in it. He had excessive thirst.

He has been in the hospital twice previously for a similar condition, the first time about a year ago, when he was admitted with a similar history occurring a few days after an excessive alcoholic bout and exposure to cold. The second time was about eight months ago, when he was in the hospital for about two weeks.

He had measles and pertussis as a child and he has had a number of attacks of gonorrhea, but he denies lues. There is no history of an infectious disease. A few years ago he had pulmonary tuberculosis and was in Asheville, North Carolina, for six to eight months, returning improved. He was quite alcoholic until eleven months ago, and he smokes excessively, consuming about twenty cigarettes a day.

This history is that of an acute nephritis occurring about one year ago, which improved under hospital treatment and has now recurred. There is no definite etiology for the condition except a New Year's celebration with exposure to cold a week previous to the onset of the original attack. There is no history of an infectious disease, but the patient has had pulmonary tuberculosis, which leads to a suspicion of a surgical lesion of the kidney.

Physical examination shows a well-nourished but decidedly anemic young man, with puffiness under the eyes and generalized edema. His chest shows no signs beyond evidence of a small healed lesion of tuberculosis at the left apex, and examination of the heart is negative. Examination of the abdomen gives no evidence of any lesion except slight edema of the wall.

The urinary output varies from 900 to 1600 c.c. in twenty-four hours, which is usually more than his daily intake of fluids. The urine, which is always distinctly cloudy, shows the pres-

ence of albumen, with a great many pus-cells and blood-cells on microscopic examination. He has a slight urethral discharge, several smears of which show a great many gonococci. On only one occasion, after numerous examinations, was an occasional hyaline cast found. His urea elimination, his ammonia nitrogen, urea nitrogen, and chlorid elimination are normal.

The blood-pressure is 160 systolic, 105 diastolic. The blood count shows red blood-cells 1,176,000, normal in appearance; hemoglobin 75 per cent.; white blood-cells 13,000; polynuclears 65 per cent.; lymphocytes 37 per cent.; large mononuclears 1 per cent.; and eosinophils 0. The patient ran no temperature while in the hospital. Repeated chemical examinations of the blood showed no evidence of retention of non-protein nitrogenous products. The figures average as follows:

Urea nitrogen	12.0
Creatinin	2.0
Uric acid	3.7
Sugar percentage	0.136

Repeated phenolphthalein tests always showed a normal elimination.

Examination of the eye grounds were quite negative. Roentgenographic examination of the urinary tract showed no evidence of calculi.

Although the general appearance of the patient strongly suggests a chronic nephritis, the only evidence of such a lesion is the albuminuria and slightly increased blood-pressure. The albuminuria, however, can readily be accounted for by the presence of pus in the urine, especially in the absence of casts. The function of the kidneys seems to be fairly normal. The presence of blood and pus in the urine would seem to indicate that the patient may be suffering from an infection of the genito-urinary tract, possibly situated in the kidney; but exact localization of the lesion cannot be determined until patient can be cystoscoped.

The history of tuberculosis and the presence of an old healed tuberculous lesion of the left lung also leads to a suspicion of a tuberculosis of the kidney, but this does not seem quite as prob-

able as a gonorrheal condition, because the urine is decidedly purulent and many gonococci are present.

The patient was kept in the hospital and his evident gonorrhea treated so as to enable the use of a cystoscope, but he left the hospital before his condition cleared up so that cystoscopy could be done.

The interesting feature of this case is the fact that the general appearance of the patient is that of a classical chronic nephritis. But the laboratory examination of the urine and blood show no evidence of a disturbed function of the kidneys nor is there any appreciable rise in the blood-pressure. Indeed, the only evidence of nephritis is the generalized edema. It is quite probable that a surgical condition of the kidney might account for this generalized edema, but while we strongly suspect it, on account of being unable to carry out cystoscopic examination we cannot positively assert that such is the case. Furthermore, a surgical condition of the kidney might also give appreciable evidence of disturbed kidney function. We are dealing, therefore, with a case of generalized edema. There is no evidence of a cardiac lesion, there is no evidence of a lesion of the blood, and there is no evidence of the kidney to account for this. On close questioning we find also that the edema is especially marked in cold weather, and disappears almost entirely in warm weather and in warm climates. Furthermore, the edema is entirely unaffected by the diet, whether it is rich or poor in salt. We are, therefore, dealing with a case of either (1) generalized angioneurotic edema, (2) a surgical lesion of one or both kidneys, or (3) chronic nephritis in such an early stage as not to give any evidence of functional disturbance of the kidney.

(*b*) **Illustrating a Problem in the Treatment of Chronic Nephritis.**—S. D., a widower, sixty-two years of age, a salesman by occupation, was admitted to the Lenox Hill Hospital complaining of frequent urination and dyspnea. The illness began four months ago with dyspnea and cough, with mucoid expectoration. For some time previous to the onset he had frequency of urination, but this has increased markedly, until at the present time he has

to get up about every two hours to urinate during the night. He can barely hold his water. Three months ago he began to have edema of the lower extremities and puffiness of the eyelids, which is gradually increasing. For the last year and a half his vision has been bad and has gradually been growing worse daily. At the present time it is so bad that he cannot read a newspaper. For the last week he has had severe headaches. He has spells of weakness, so that he cannot get up out of bed; at such times he is unable to walk, falling down when he attempts to do so, and then he is unable to get up again. He has lost about 40 pounds in weight in the last four weeks. About five months ago he had a hemiparesis. He had diabetes four years ago with carbuncles as a complication. He had measles, typhoid, and pneumonia as a child, and heart and kidney trouble about a year and a half ago. He denies lues. One brother died of apoplexy and another of intestinal tuberculosis.

Examination gives the impression of a considerable loss in weight. There is no evidence of general glandular enlargement. The head shows no evidence of any lesions except for the tortuous temporal vessels. The eyes show pallor of the conjunctivæ; the pupils are equal and react both to light and accommodation; the fundi are pale and show a progressive optic atrophy with slightly tortuous vessels; there is no evidence of an albuminuric or diabetic retinitis. There are no evidences of any lesions of the nose, throat, or ears. The tongue is coated and the teeth are in very poor condition.

The chest is barrel shaped and the lungs show the characteristic emphysematous breathing with occasional sibilant râles. The heart is enlarged, the apex-beat being in the sixth interspace 12.5 cm. to the left of the median line. The heart sounds are regular, rhythmic, but faint and distant. There is a suggestion of a distant faint systolic murmur to be heard at the apex, which is not transmitted however. The pulse is regular, full and bounding, and there is evidence of arteriosclerosis in the palpable vessels. The blood-pressure is 145 systolic and 80 diastolic.

The abdominal wall is soft and flabby. The liver border is felt about three fingerbreadths below the costal margin and is

tender on pressure. The spleen is not palpable. There is no evidence of free fluid in the abdomen. No abnormal masses can be felt. There is a scrotal hernia on the right side. The extremities show no evidence of any lesions. The knee-jerks are absent on both sides. There is evidence of an old right hemiplegia. Rectal examination shows a markedly enlarged prostate. The Wassermann reaction is negative. The daily urinary output varies from 800 to 1300 c.c., which is usually about the same amount as the total fluid intake.

The urine examination always shows a specific gravity varying from 1015 to 1021, a faint trace of albumen, no sugar, and microscopically many pus-cells and occasional hyaline and granular casts. The phenolphthalein tests average from 25 to 48 per cent. The blood examination shows a non-protein nitrogen retention, as the following figures indicate:

Urea nitrogen	83.0
Creatinin	3.7
Uric acid	3.7
Sugar percentage	0.192

The history is that of a cardiac syndrome either primary or secondary to a kidney lesion. There is no definite etiologic factor in the history that indicates whether the heart or kidney was the most probable primary lesion. The marked frequency of urination suggests a lesion of the prostate, and the occurrence of a mild attack of hemiplegia suggests a vascular lesion.

The physical examination shows a rather well-nourished but anemic and stupid old man, who gives evidence of a chronic nephritis, an arteriosclerosis, and a secondary myocardial insufficiency. He also has an old hemiplegia on the right side and quite a large prostate. It is difficult to find any definite etiology for his lesions, but it would seem that the old age and the typhoid and pneumonia are the most important factors. The lesion from which the patient is evidently suffering is situated in the kidneys, and it is evidently a chronic nephritis.

We therefore attempted to determine what was the functional disturbance of the kidney. There is no evidence of any edema,

consequently there is no salt retention. The daily urinary output is normal, consequently there is no water retention. The chemical examination of the blood shows evidence of a retention of non-protein nitrogenous products, as is shown by the increase in the urea, creatinin, and uric acid percentages. The dull, lethargic, stupid mentality may be considered evidence of a mild uremic state which is associated with the non-protein nitrogen retention.

The case therefore presents a problem in treatment. What we have to treat is the nitrogen retention. This we can do by eliminating the proteins from the diet so as to lessen the formation of protein waste products, and increasing at the same time all the excretions of all his excretory organs. Instead of reducing the proteins in his diet, by gradually eliminating the protein foods we attempted to determine the amount of proteins the patient could stand without inducing retention, at the same time maintaining his caloric needs. This was done in a manner similar to the Allen treatment of diabetes. The patient was starved for three days, receiving only 16 c.c. of whisky every four hours, and coffee and lemonade up to 500 c.c. daily. The only medication was sodium bicarbonate, 0.6 gram, three times a day. The lemonade and sodium bicarbonate were given for the purpose of preventing a possible acidosis which the starvation might produce. At the end of the three days' starvation another chemical examination of the blood was done. This showed a marked reduction of the nitrogen retention, as the following figures indicate:

Urea nitrogen	20.8
Creatinin	1.85
Uric acid	2.0
Sugar percentage	0.126

The patient was then put on a milk-diet of 500 c.c. for about three days. This contained about 35 grams of protein. A chemical examination of the blood was again done, and it showed no increase in the previous figures.

We then added spinach, baked potatoes, toast, broth, ice-

cream, and orangeade, so that the patient was getting about 60 grams of proteins, about 1960 c.c. of fluid; and the caloric value of this diet was about 1640. This was kept up for about a week, when a chemical examination of the blood was done again, but it showed no increase in the last figures. We then added string beans and increased the milk to 750 c.c., raising the proteins to 80 grams, the fluid to about 2500 c.c., and the calories to about 2200.

The only medication during this time was sodium bicarbonate, 0.6 gram, three times a day, magnesium sulphate 30 grams every morning to increase the elimination by the intestinal tract, and tincture of digitalis 0.6 mil. for the dyspnea and to improve the circulation in the kidney.

At the end of this time another chemical examination of the blood was done, but it showed no evidence of nitrogen retention.

The patient gradually improved, his stupid, dull, lethargic state disappeared, he gained in weight. This diet was kept up for about two months, the patient finally being discharged improved. His final blood condition showed no evidence of nitrogen retention. His urinary condition, however, remained the same, albumen and casts still being present, but his phenolphthalein tests showed a higher functional ability of the kidneys.

This case is interesting because it is a type of chronic nephritis in which the main functional disturbance in the kidney is in its inability to eliminate nitrogenous waste products, and because we were able to improve the condition by determining the protein tolerance and keeping the patient on such a diet. The patient was suffering from a mild uremia. The uremic state cleared up when the nitrogen retention was reduced by the elimination and subsequent reduction of the proteins in the diet. The tolerance for proteins, which was higher than the normal average requirements, was determined by beginning with starvation and then gradually increasing the amounts while maintaining his caloric needs.

It is interesting to note that the albumen and casts in this case have no relation whatever to the amount of protein intake.

It seems that they are merely evidences of a nephritis, but they do not indicate anything in regard to the ability of the kidney to eliminate protein waste products.

(*c*) **Illustrating a Problem in Prognosis and the Effect of Decapsulation.**—M. M., a carpenter, thirty-six years of age, born in Ireland, married, was admitted to the Lenox Hill Hospital complaining of swelling of the arms, legs, abdomen, and puffiness of the face for a week previous to admission. There was slight dyspnea, but no disturbance of vision and no vomiting. About one year ago he had a similar attack, in which the dyspnea on exertion was more marked, and, in addition, he had failing vision, polyuria, and frequent urination. He continued under treatment for the year following this attack. He has never had any other illness except for frequent attacks of tonsillitis. His occupation made it necessary for him to be out in the cold in the open constantly and he has been a heavy drinker, taking 5 glasses of whisky a day and about 5 glasses of beer. He denies gonorrhea and syphilis. There is nothing relevant in his family history except that his father died of dropsy.

The patient on admission presented the appearance of a fairly well-nourished but quite anemic middle-aged man, with puffiness of the face and typical generalized edema which suggested at once chronic nephritis. There was nothing abnormal in the head or any of the cranial cavities until the eyes were examined, when it was found that although the reaction to light and accommodation were both normal, he had a slight external strabismus and a nystagmus. The chest was normal and there was no evidence of any lesion in the lungs. The heart, however, was enlarged to the extent that the left border extended about two fingerbreadths to the left of the left nipple line, and the apex-beat was heard best in the sixth interspace in the left nipple line. The heart sounds were of poor muscular quality, though they were normal in rate and rhythm. There were no murmurs to be heard, but the second aortic sound was rather faint and muffled.

The abdomen showed no evidence of any lesion and the contained viscera were found to be normal. The blood-pressure

varied from 190 to 210 systolic, with a diastolic of 108 to 116. There was no evidence of arteriosclerosis of the palpable vessels.

The urinary output was within normal limits, varying from 1000 to 1800 c.c. in twenty-four hours, which was usually more than the daily amount of fluid intake. The urine varied, at times being acid and at other times being alkaline in reaction; its specific gravity averaged between 1009 and 1017, it usually contained large amounts of albumen, never any sugar, at times many hyaline and granular casts, and always more or less pus-cells. The phenolphthalein test showed only a faint trace on every examination.

The chemical blood examinations showed a non-protein nitrogen retention; the urea varying from 50 to 63, the creatinin from 7 to 9, the uric acid about 4 to 4.5, the sugar percentage 0.146, and the cholesterol from 150 to 152. The Wassermann reaction of the blood was negative.

This history is that of a classical chronic nephritis which came on suddenly about a year ago. The only factors in the history that we might consider of etiologic value are the occupation, which constantly exposed the patient to cold, and the very marked history of alcoholism. The positive findings all point to the kidneys as the seat of the primary lesion. The case is evidently that of a chronic nephritis with indications of a non-protein nitrogen retention and marked anasarca. In other words, the kidney is unable to eliminate protein waste products and salts. The water elimination seems to be fairly good.

The important symptoms to be treated in this case were the nitrogen retention and the salt retention. Since the evidence of nitrogen retention was very marked, this was the most important condition to treat because the patient's outcome depended largely on this, as uremia was threatening. His edema did not inconvenience him very much. Furthermore, the edema was a simple matter to eliminate, either by limitation of fluids or by a salt-free diet. An attempt, therefore, was made to treat the nitrogen retention by determining his protein tolerance in the same manner as in the previous case. But even when the patient was on starvation for about five or six days the chem-

ical examination of the blood showed no diminution of his retention; the only result was a loss in weight and a slight diminution in the creatinin from 9 to 7. We increased the protein intake by giving the patient milk and overfeeding with carbohydrates, allowing a diet containing about 60 grams of protein, but this had no appreciable effect upon the nitrogen retention, so that we abandoned this method of treatment and determined to treat the patient rather as an individual, our object being only to make him comfortable, not limiting his diet in any way, and increasing the excretion through all the excretory channels by saline purgatives and by digitalis. The edema gradually subsided and the patient felt better. Consequently, we came to the conclusion that this was a case of chronic nephritis with a persistent disturbance in the function of the kidney so that it was unable to eliminate protein waste products and salts.

The prognosis, therefore, according to the very high nonprotein nitrogen figures was very dubious. The patient was doomed to suffer from persistent disability of his kidney, and in all probability would not live longer than a year or two. The persistent high figures of creatinin in the blood corroborated this assumption.

We therefore decided to attempt to do a decapsulation of the patient's kidneys and give him the benefit of whatever good effect this operation would have. Consequently, one month after admission, the patient was transferred to the surgical service of Dr. Herman Fischer, and the following day a decapsulation of both kidneys was performed under ether anesthesia. The kidneys at operation were seen to be typically small and contracted.

The patient made an uneventful recovery from the operation. His urinary findings after the operation did not vary from those before, nor did any of the subsequent phenolphthalein tests show any increase in the functional capacity of the kidneys. A week after operation the blood findings were as follows:

Urea nitrogen	77.0
Creatinin	9.0
Uric acid	4.4
Sugar percentage	0.168
Co_2 combining power	50.0

In other words, the nitrogen retention in the blood was not changed. Twelve days later another blood examination showed

Urea nitrogen	50.0
Creatinin	5.4
Uric acid	3.3
Sugar percentage	0.152

This shows a slight improvement in the function of nitrogen elimination, as is indicated by the slight diminution of the creatinin elimination.

The patient gradually improved, his edema subsided, and he left the hospital about three and a half weeks after the operation feeling very comfortable, but with evidences of a nitrogen retention in the blood and a consequent failure to eliminate protein waste products.

This case is interesting because it shows that with persistent high blood figures of nitrogen retention, especially the high creatinin figures, the prognosis is bad because the nitrogen retention cannot be changed, and we cannot hope to gain much from regulation of diet. The patient should merely be made comfortable and any contingency should be treated as it arises. If uremia occurs, this must be treated in the usual way; if a myocardial insufficiency occurs, this should be taken care of. As far as the ultimate outcome is concerned, little is to be expected. The decapsulation operation in this case did not result in any appreciable improvement in the ability of the kidneys to eliminate protein waste products.

IV. TWO CASES ILLUSTRATING THE DIAGNOSIS OF AORTIC SYPHILIS

(*a*) **Early Aortic Syphilis.**—L. M., a widowed coachman, sixty-three years of age, was admitted to the Lenox Hill Hospital complaining chiefly of swelling of the legs of two weeks' duration.

The illness began about two weeks before admission, when he began to notice that he was short of breath and that his legs and abdomen were gradually getting swollen. At the same time he

would cough at night and suffer from severe frontal headache. He has attacks of precordial pain which radiate up to his left shoulder and down the left arm. These attacks have occurred even for some time before the onset of the present illness. Of late his vision has been blurred and he has had marked frequency of urination during the day, and he has had to get up about five or six times a night to urinate. He has lost about 75 pounds in weight during the last few years.

He had measles as a child, as well as frequent attacks of sore throat and joint pains. For the past eight years he has been suffering from heart and kidney trouble. He denies lues, but he had gonorrhea about forty years ago.

He is a man of good habits, except that he drinks a glass of beer occasionally and smokes several pipes of tobacco daily and an occasional cigar.

The history is that of a cardiac syndrome, either primary or secondary. A primary vascular lesion of the heart is strongly suggested by the frequent anginal attacks. There is no definite etiologic factor to account for his condition except possibly the rather indefinite history of sore throat and joint pains.

The patient is a well-nourished old man, who is slightly dyspneic on lying down. There is no evidence of any lesion until the chest is examined. Here the dulness, diminished breathing, and the distant fine subcrepitant râles at both bases of the lungs behind, especially on the left side, strongly suggest the presence of fluid. The heart is enlarged, the left border extending to about a fingerbreadth to the left of the left nipple line. A diastolic murmur may be heard at the base, and it is transmitted upward to the left side of the neck and downward and to the left of the apex.

The abdomen shows no evidence of fluid or any lesion. The liver border, however, may be felt indistinctly about three fingerbreadths below the costal margin. There is no edema of the scrotum or lower extremities. The blood-pressure was 165 systolic and 50 diastolic. The Wassermann reaction of the blood is 4 plus. The urine analysis is negative. The phenolphthalein test shows 27 per cent. The chemical examination of the blood

shows no evidence of nitrogen retention. The roentgenographic examination of the chest shows only evidence of an enlarged heart.

The clinical evidence is that of an aortic regurgitation with anginal attacks on a syphilitic basis. The positive evidence of syphilis, in addition to the attacks of pain, evidently anginal in character, proves the presence of a syphilitic aortitis. In spite of the negative *x*-ray evidence of a dilatation of the aorta this lesion has evidently produced a sufficient dilatation of the aortic ring so that a regurgitation through the semilunar valves is produced. This valvular lesion is now decompensated and the patient is suffering from a myocardial insufficiency.

As regards treatment, the patient should receive intensive treatment with mercury and iodids for about six to eight weeks, and then salvarsan may be given. We never know the exact nature of the pathology of the aortic lesion. Consequently, it is not wise to give salvarsan even when there is a remote possibility of breaking down a syphilitic lesion in the aorta, which might be a fresh one. When salvarsan is given in such cases it should be given in very small quantities of fluid so as to avoid producing a sudden rise in blood-pressure.

(*b*) **Aneurysm of the Arch of the Aorta.**—E. A., a plasterer, sixty-three years of age, unmarried, was admitted to the Lenox Hill Hospital complaining of shortness of breath and swelling of the legs and scrotum for three months.

The illness began about a year ago, when he gradually began to have shortness of breath on slight exertion. At times he would have edema of the legs and face in the evening. He has had to be confined to bed for a few weeks six times in the course of the last year. He now comes to the hospital on account of shortness of breath, edema of the extremities, and cough at night.

At the age of three he suffered from eye trouble, the principal symptoms of which were "spots before the eyes." In a few years the symptoms disappeared. He has never had scarlet fever. Although he has been having attacks of sore throat

every winter, he has never had an attack of rheumatism. He had a gonorrhea when he was twenty, and two years later he had a hard chancre followed by a rash.

Except for moderate beer drinking, averaging about 6 glasses a day, and one or two pipes of tobacco daily, he is a man of fairly good habits.

His father died of stomach trouble at the age of fifty. Besides this there is nothing relevant in his family history.

The history of this patient is apparently that of a myocardial insufficiency probably the result of a primary or secondary heart lesion. From the fact that a definite history of lues is present, a primary lesion in the aorta should be strongly suspected.

The patient is a rather plethoric, heavily built man with a characteristic rosacea of the face, and suffering from severe dyspnea. He is markedly cyanotic. There is a generalized edema of the lower extremities, abdominal and thoracic wall extending upward to the level of the scapula.

His chest is barrel shaped and gives a hyperresonant note all over except at the left base behind where the decided dulness, diminished fremitus, and bronchial breathing strongly suggest fluid. The mediastinal area of dulness is widened to about twice its normal width. It merges with the cardiac area of dulness in an obtuse angle on both sides. The area of cardiac dulness is widened. Its border extends on the left to the anterior axillary line, where, in the fifth interspace, the apex-beat may be heard. The right border extends to the right to about two fingerbreadths to the right of the sternum and obliterating the cardiohepatic angle. The heart sounds can be heard best in the fourth and fifth interspaces around the left nipple, but they are distant and muffled. No murmurs can be heard anywhere (Figs. 225, 226).

The pulse is small and evidently paradoxic in character, and there is distinct evidence of arteriosclerosis in the palpable vessels.

The abdomen is distended, the abdominal wall is edematous, and free fluid is present in the abdominal cavity. The liver border may be felt about three fingerbreadths below the costal

margin, but its consistency is normal. The lower extremities are edematous and old healed ulcers are present in both legs.

The daily urinary output is normal, and the urine has a specific gravity of about 1027 to 1030, and always contains a faint trace of albumen, no sugar, and at times many small hyaline casts.

Fig. 225.—Roentgenogram (anteroposterior view) of chest of E. A., showing aneurysm of arch of aorta, pleural and pericardial effusion. Case of aortic syphilis with aneurysm of arch of aorta.

A phenolphthalein test (catherized specimen) could not be done because of a markedly tortuous urethra. The chemical examination of the blood, however, showed only a slight retention of uric acid.

The systolic blood-pressure was 145 and the diastolic 95. The Wassermann test of the blood was negative.

The roentgenographic examination of the chest showed an aneurysm of the beginning of the arch of the aorta, and a very large heart shadow, with possible evidence of fluid in the pericardium and in the left chest.

Fig. 226.—Roentgenogram of chest of E. A., showing lateral view of aneurysm of arch of aorta. Case of aortic syphilis with aneurysm of arch of aorta.

The very severe dyspnea and cyanosis and pleural effusion, together with the generalized edema, are evidences of a myocardial insufficiency. The cardiac signs, however, are those of a pericardial effusion, which is evidently secondary to an aneurysm of the arch of the aorta. The evidence pointing to an aneurysm of the arch of the aorta is the widened area of cardiac dulness

and the evidence of the roentgenogram. The Wassermann reaction is negative, but the definite clinical history of lues is just as valuable in determining the etiology as the Wassermann test.

It is interesting to note that the usual physical signs of aneurysm of the arch of the aorta are absent. This is due to the presence of a pericardial effusion, the emphysema of the chest, and to the location of the aneurysm at the very origin of the aorta, as is shown by the roentgenogram. It is an interesting speculation to decide whether the pericardial effusion is due to the aneurysm or to the myocardial insufficiency. While we have no evidence to decide this point, we can, however, logically explain the effusion by the dilated aortic ring pressing on the coronary veins with a consequent stasis and pleural effusion.

CLINIC OF DR. A. McI. STRONG

Presbyterian Hospital

AURICULAR TACHYCARDIA IN CHILDREN: 2 CASES

The paroxysmal tachycardias have thus far defied exact etiologic classification. Indeed, it is doubtful if they are susceptible of etiologic classification except in a manner too uncertain to be of practical value, for the functional and the organic appear to be inextricably bound together in their causation.

The usual criteria of true paroxysmal tachycardia are as follows: A very rapid and usually, though not always, regular ventricular rate, abrupt in its onset, and frequently accompanied by the subjective sensation of palpitation. The rate is seldom less than 160, and is often as high as 300 or more. The termination of a paroxysm is characteristically abrupt, and may be followed immediately by a pause similar to the compensatory pause seen after a single premature contraction.

There are four types of abnormal rhythm which may be responsible for the paroxysm. They are: auricular tachycardia, auricular flutter, auricular fibrillation, and ventricular tachycardia. At present we are concerned only with the first three. Of these, the first two are the disorders most frequently associated with paroxysmal tachycardia. With the more extensive use of the string galvanometer, however, it has become evident that auricular fibrillation occurs in paroxysms far more frequently than was formerly supposed.

In a large proportion of cases these rhythms are associated with disease of the myocardium; and yet case reports are not lacking to show that any one of them may have a functional or a toxic origin. Hence we are unable to state, in a given case, *from the rhythm alone*, whether or not organic disease of the heart is

present. In the last analysis our decision in regard to the heart does not rest with the rhythm any more than it rests with a murmur in a case suspected of valvular disease. Always we are compelled to seek the final answer in other data, such as the age of the individual, his habits, past or present, infections, the frequency and duration of the paroxysms, the size and form of the heart, the condition of the valves, of the arteries, the blood-pressure, the adequacy of the peripheral circulation, the state of other organs, as the kidney and the thyroid gland.

The three types of tachycardia mentioned as having their point of stimulus formation in the auricle have this in common —they are all ectopic rhythms. The cardiac pacemaker is no longer situated in the sino-auricular node, but in some other region of the auricular musculature which, by virtue of increased irritability or superior rhythmicity, has vicariously assumed the function of pacemaker for the time being, or even permanently.

In auricular tachycardia the heart responds to stimuli from a single ectopic pacemaker in the auricle, and the ventricle responds to every auricular impulse. That the rhythm is an ectopic one may be demonstrated by the string galvanometer. The P deflection of auricular activity assumes an abnormal form until the paroxysm terminates. The auricular rate is usually less rapid than in auricular flutter, and in the last-named rhythm the ventricle does not respond to every auricular impulse.

The 2 cases about to be described belong to the category of auricular tachycardia, and demonstrate two contrasting clinical types of this condition. Both were under ten years of age. In neither case was it possible to determine with certainty the etiology of the disorder. In one case there was a tendency to spontaneous recovery, apparently with permanent restoration of the normal rhythm. In the other there was not only no tendency to spontaneous return of the normal rhythm, but the tachycardia resisted stubbornly all therapeutic measures, was eventually complicated by evidences of myocardial insufficiency, and ultimately contributed to the fatal outcome of an acute infection. In general, it may be said that the tachycardias of this class are more prone to resist all efforts to slow the heart than are those

of the other two classes, *i. e.*, auricular flutter and auricular fibrillation. Flutter quite commonly responds to digitalis therapy by slowing of the ventricle and ultimately resumption of the normal rhythm. Fibrillation usually responds by slowing of the ventricle alone.

CASE I.—A schoolgirl, nine years of age. Home conditions good. Coffee once a day. Family history irrelevant.

Past History.—Diphtheria and measles four years ago. Tonsils "removed" four years ago. Had been subject to frequent sore throat. Occasional toothache; no joint pains. Has never experienced dyspnea on exertion. One attack of rapid heart action three months ago; disappeared after two days' rest in bed. Not noted whether it ceased gradually or suddenly.

Present History.—Yesterday felt quite well until 11.30 A. M., then felt her heart begin to beat very rapidly. Soon after the onset she went to bed, and soon felt better. That night she vomited three times. No chills, no headache, no pain of any kind; merely nausea and anorexia. The following day she felt better, though the rapid heart action continued. She walked to the dispensary and was admitted to the hospital. Her pulse when she arrived at the dispensary was 240.

Physical Examination.—A well-nourished, healthy looking child, without evidence of discomfort or circulatory insufficiency. Teeth badly cared for, but no decayed roots and no pyorrhea. Tonsils slightly enlarged, but clean. No enlargement of superficial lymph-nodes. *Chest* well formed and symmetric. Respiratory movements normal. *Lungs* clear. *Heart:* Right border 1.5 cm., left border 8 cm., from midsternal line. Point of maximum impulse in the fifth interspace 6 cm. from midline. Impulse diffuse. Action very rapid (216), but perfectly regular. No thrill palpable, no diastolic shock. First sound of fair quality; no murmurs present. No accentuations of valve sounds and no reduplications. *Pulse* small, weak, and very difficult to count. *Abdomen:* Liver, by percussion, from fifth interspace to costal margin; edge not palpable. Spleen not enlarged. *Extremities:* No edema. Reflexes normal. *Temperature*, 101.4° F. *Weight*, 70¼ pounds. *Teleroentgenogram:* Length of heart 11 cm.;

extreme borders 3.7 cm. to the right, 5.3 cm. to the left, total transverse diameter, 9 cm.

Leukocytes, 16,000; polynuclears, 74 per cent.; lymph, 34 per cent.; eosinophils, 1 per cent.; transitionals, 1 per cent. Wassermann reaction negative.

Course.—The child received no medication throughout her stay in the hospital except one dose of castor oil on admission. Her temperature fell to normal on the second day and remained so throughout. She was put on soft diet and kept in bed for

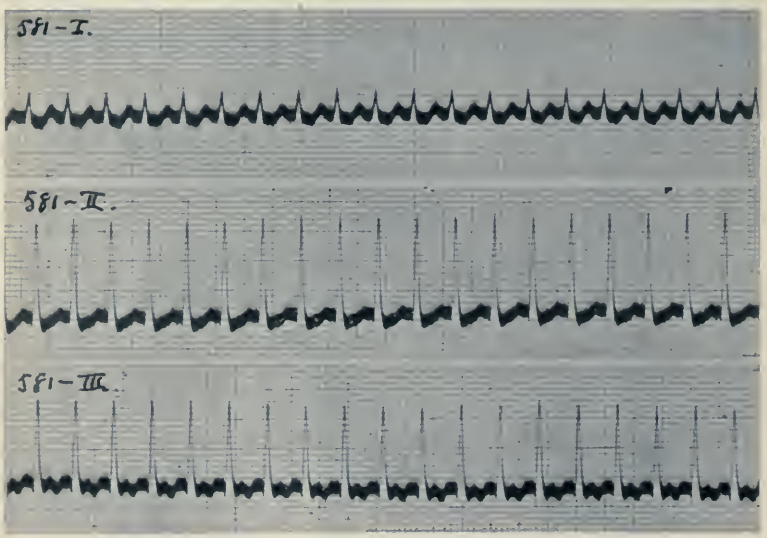

Fig. 227.—Electrocardiogram of Case I during the period of tachycardia.

several days. On the second day her pulse was 148; on the third day, 78; fourth day, 82; and on the tenth day, just before her discharge from the hospital, 90. The heart action remained perfectly regular throughout.

Over a period of seven months after she was discharged from the hospital the child made twenty-four visits to the dispensary for observation. Usually she admitted some constipation, and once had a sore throat, but usually there were no complaints of any kind. During the first month after leaving the hospital

she had noticed a few short periods of rapid heart action. The last visit was on February 13, 1919. She was perfectly well, and weighed $83\frac{3}{4}$ pounds.

The Electrocardiograms, Fig. 227 (taken on day of admission).—The heart rate is 221. The P wave is difficult to identify with certainty; apparently it is inverted in Lead III. The P–R interval as estimated from the apparent foot-point is about 0.14 second. Although the inverted P in Lead III is not enough alone to justify the assumption that the rhythm is an ectopic

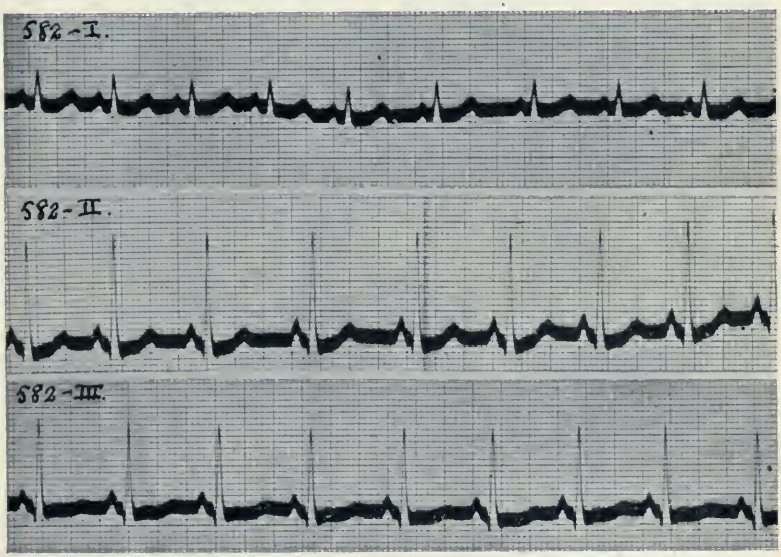

Fig. 228.—Electrocardiogram of Case I after the resumption of the normal sinus rhythm.

one, the record is, in appearance, very characteristic of auricular tachycardia, and the rate itself speaks very strongly for this interpretation.

Figure 228, taken on the second day, shows reversion to the normal sinus rhythm. The rate is 88. The P wave is upright throughout, and the P–R interval measures 0.12 second. This record establishes the fact that the previous rhythm was of ectopic origin, and belonged in the class of paroxysmal tachycardia commonly known as auricular tachycardia.

Discussion.—In this case we have no positive evidence of organic disease of the heart. To state categorically that the heart is normal, however, would be to assume a knowledge which we do not yet possess. It is by watching such individuals for as long a time after the attack as possible that we may eventually learn the significance of the disordered rhythm.

Case II.—A schoolgirl aged five years. Normal birth and feeding, normal development. Home conditions good.

Family History.—Father alcoholic; said to suffer from rheumatism. Mother had one miscarriage at two months. Two other children living and well.

Past History.—Chickenpox three and a half years ago. Has had German measles. Always subject to colds, which are invariably accompanied by sore throat. During the past year and a half has had three severe attacks of follicular tonsillitis. No rheumatic fever, no joint pains.

Present Illness.—About seven weeks ago, following playhour at school, the teacher noticed that the child looked pale and ill. The school physician said the child had a "rapid heart" and advised sending her to a dispensary. From the dispensary she was sent home, with some medicine, and directed to remain in bed. She did so for three weeks, but the pulse continued at 170 to 180 day and night. It never fell below 150. For the next four weeks the child was up and about, playing as usual, but was very easily fatigued, especially after climbing stairs. The mother thought she was dizzy at times. No headache, no nausea or vomiting, appetite and bowels normal, no pain. She herself did not seem to be conscious of the rapid heart action.

Physical Examination.—A pale, well-developed, fairly well-nourished child, without dyspnea or evidence of any discomfort. She walked into the hospital ward. *Mouth:* Four carious teeth; tonsils large and red. *Neck:* A few small cervical and submaxillary nodes palpable. *Chest* outwardly normal. *Lungs* clear. *Heart:* Right border 3 cm., left border 7.5 cm. from the midsternal line. Point of maximum impulse in the fifth space, midclavicular line; diffuse in character. Action regular, rapid (180). The sounds of good quality; no murmurs or accentuations.

Teleroentgenogram: Length of heart, 11.5 cm. Extreme right border 3.5 cm., extreme left border 7.3 cm. from midline; total transverse diameter 10.8 cm. *Abdomen:* Liver palpable at costal margin; spleen not felt. No tenderness present. *Extremities* normal. Reflexes normal. *Temperature* 98.6° F., *respirations* 44; later 28. A throat culture was negative for Klebs-Löffler.

Fig. 229.—Teleroentgenogram of Case I.

Leukocytes, 11,200; polynuclears, 51 per cent.; lymphocytes, 47 per cent.; transitionals, 2 per cent. Urine was normal (Fig. 229).

Course.—On the second day the pulse was once found to be 92; a little later, 180. On the third day it was 192, always regular. That night, while sleeping, 145.

The patient was given soft diet and kept as quiet as possible.

On the ninth day after admission tincture of digitalis was begun in the hope of slowing the heart. It was given for fifteen days in gradually increasing doses, beginning with 6 minims on the first day. By the end of fifteen days she had received approximately the equivalent of 1 gm. of the powdered leaves. At this point the ventricular rate became a little slower and irregular, due to partial heart-block (digitalis). Vagus pressure had been shown to exercise the same effect. The auricular rate showed

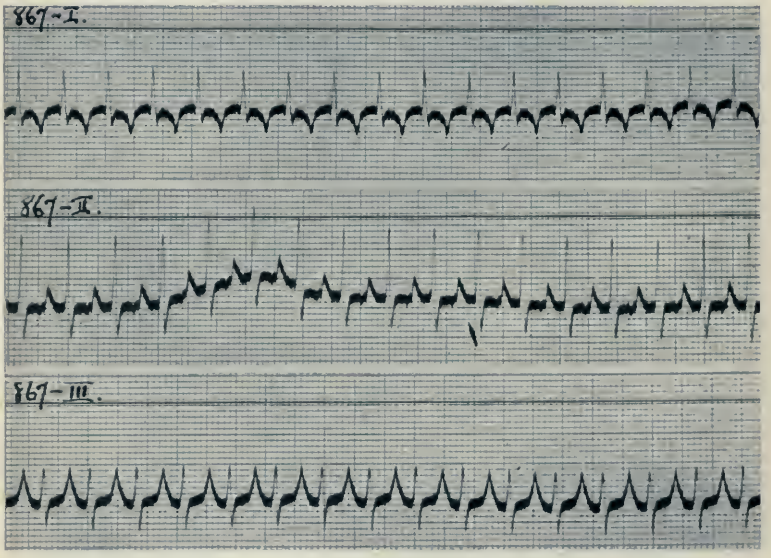

Fig. 230.—Electrocardiogram of Case II: P inverted in Lead I; summation of P and T in Lead III.

only a slight change—*i. e.*, from 190 to 180. The heart recovered promptly from the effect of the digitalis, and the child was discharged from the hospital nine weeks after admission. Her pulse ranged from 180 to 150, always regular; her temperature was normal, and she felt quite well, though rather easily fatigued.

For nine weeks after her discharge she was kept very quiet and had no subjective symptoms save an occasional dizzy spell. There was no evidence of cardiac incompetence during this period. The heart remained rapid—up to 190. Thirteen weeks

after discharge she returned to the dispensary. She had been running about a good deal, and became dyspneic on relatively slight exertion. Her temperature had remained normal. On examination, the heart showed a systolic murmur at the apex, transmitted to the axilla. The lungs showed moist râles at both bases.

Seven weeks later she returned to the dispensary for the last time. She had been kept very quiet, according to instructions,

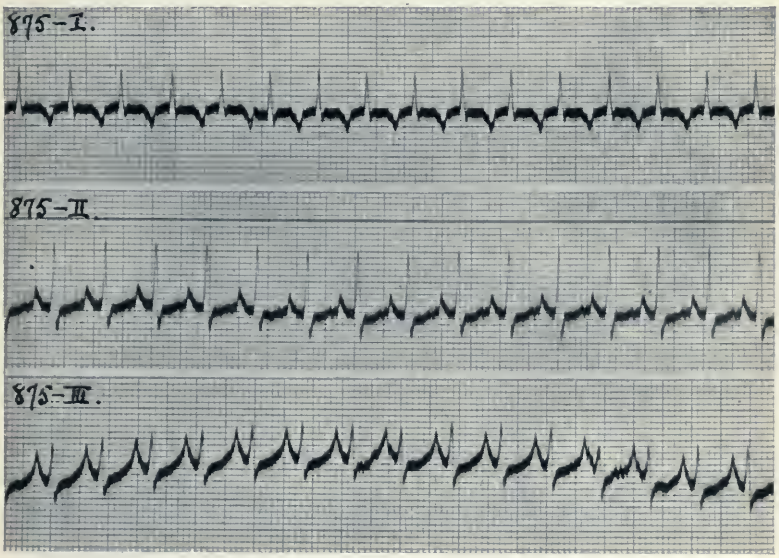

Fig. 231.—Electrocardiogram of Case II, showing slight changes in initial complexes which might be interpreted as indicating progressive right-heart hypertrophy.

but the rapid heart action, and the dyspnea on slight exertion had persisted. The left border of the heart was found 1 cm. farther out than before, and the systolic murmur and râles at the bases of the lungs were still present. Three weeks after the last visit the child died of pneumonia complicated by heart disease, as stated by her physician.

Electrocardiograms, Fig. 230 (two days after admission to the hospital).—The rate is 190, the ventricle responding to every au-

ricular impulse. There is some evidence of muscular preponderance of the left side of the heart. The striking features are the inverted P wave in Lead I, with the apparent summation of P and T where there is any evidence of a T wave. The P–R interval is either 0.14 or 0.18 second, according to the point chosen as the correct foot-point of P.

Figure 231, sixteen days after admission: She had received the equivalent of 0.3 gm. digitalis leaves in seven days. There is

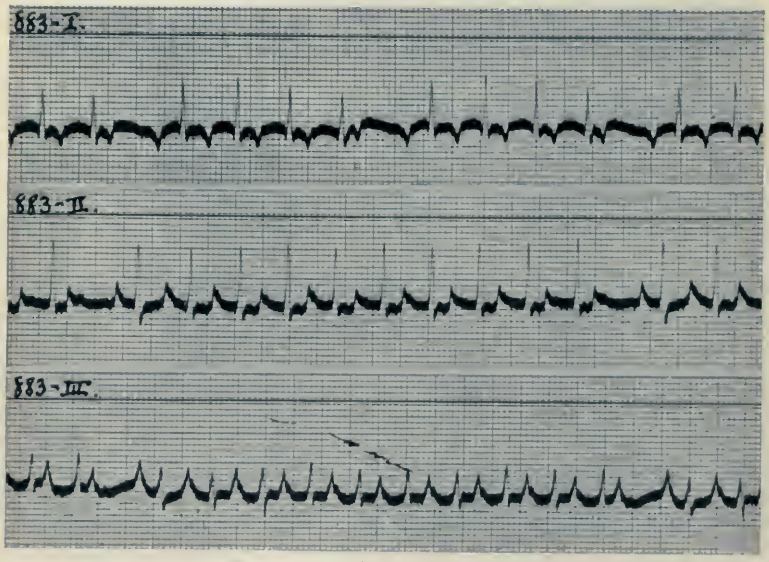

Fig. 232.—Electrocardiogram of Case II at the time of digitalis block, revealing the form of P when not modified by interference. The alterations in the initial complexes pointed out in Fig. 231 are still more marked here.

little if any significant change, unless the slight alteration in the relative amplitude of R and S in Leads I and III be taken to indicate a change in the muscle preponderance on the two sides of the heart. This, however, is a point of interest in connection with Figs. 230 and 232.

Figure 232, three weeks after admission: Partial heart-block due to digitalis, of which she had received about 1 gm., in terms of leaves, in two weeks. The auricular rate remains practically

unchanged (180), and the form of the auricular complex remains essentially as in the first record. There are changes in the relative size of the R and S waves, to a more marked degree than in Fig. 231. It would be hazardous to interpret these as indicating a change in the relative muscular preponderance when the heart

Fig. 233.—Teleroentgenogram of Case II.

is under the influence of digitalis. This record is of value in that the P wave is extricated from other complexes by reason of the block, thus enabling us to identify it (Fig. 233).

Discussion.—In this case we are dealing with a tachycardia originating in the auricle and persisting in spite of all measures aimed to slow the heart. Both vagus pressure and digitalis,

which have been found effective in a certain number of these tachycardias, failed to affect the rate of the pacemaker, merely inducing depression of conduction at the junctional tissues. We have not as good evidence of an ectopic source of the rhythm as in Case I, since there is no change in the mechanism while under observation to serve as a basis for comparison. The constant high rate and the inverted P in Lead I are the points which favor the supposition that the rhythm is ectopic.

The matter of most importance in this case is the striking exhaustion of the cardiac reserve under the rapid rhythm. Whether we attribute this to fatigue due to so rapid a rate over a period of one year, or to primary disease of the myocardium, the condition was undoubtedly an important factor in lessening the child's chances against the terminal infection. The most reasonable supposition is that a primary myocardial lesion, due to some previous infection, determined the abnormal rhythm, and that myocardial exhaustion contributed toward the final outcome. In the one year of illness the heart probably expended the energy which should have been distributed over a period of two years or more.

Summary.—Two cases of auricular tachycardia in children are described. One of them, by reason of its transitory character and the absence of clinical evidence of any other cardiac disorder, as well as by reason of the subsequent history, was, in all probability, functional. The other, because of its persistence in spite of all efforts to abolish it, and because of its association with definite evidence of cardiac injury, must certainly have had an organic basis. That the first one represents an ectopic rhythm there can be no doubt. That the rhythm in the second case also was ectopic seems highly probable.

CLINIC OF DR. DANA W. ATCHLEY

Presbyterian Hospital

RENAL DISEASE

Study of Renal Function. Practical Application of the Kidney Activity to Clinical Material. Prognosis. Treatment. Presentation of Cases.

March, 1919.

There are some diseases where we are fortunate in having a perfectly known cause that leads to a comparatively definite series of events; a discussion of typhoid fever, for example, should fix in the mind of the student a well-established picture of onset, course, and common variations. But certain other diseases are in no way made to order, for they show marked differences between individuals, and we are confined to the presentation of a point of view, a method of attack; diabetes is obviously such a disease. Nephritis has been too long taught as a disease of the first category, and many narrow groups have been presented, each with its supposed clinical picture. Practically, such grouping is impossible and is more often confusing than helpful to the student. Each case of renal disease is a distinct entity, and may be properly understood only after a certain minimum amount of material has been gathered. This material will suggest the prognosis and treatment in the case under study, but will fit the case into no neat pigeon-hole. Before I discuss the accumulation and interpretation of the essential data in a case of renal disease brief mention should be made of the most rational classification that has been proposed, merely because the student demands some cataloguing, and a complete refusal may discourage interest.

In the absence of an etiologic basis, and when the pathologic and clinical pictures show uncertain coincidence, the most logical basis of classification must be physiologic. Widal first suggested the groups—salt retention, nitrogen retention, and mixed type. There is undoubtedly a clinical syndrome in which the predominant functional disturbance is an inability to excrete sodium chlorid, and there is also another picture with nitrogen retention a marked feature, but the "pure" cases, if we may speak of them as such, are very infrequent in comparison with the cases where there is a combination of the two so-called types. In spite of this criticism Widal's classification seems to be the best yet proposed, and is sufficient when hasty, casual description of cases is all that is required. It is to be recommended to those who desire a more particular terminology than the comprehensive term "renal disease."

The accumulation of data in renal disease is so very important and there have been so many and varied contributions, that a rather detailed discussion may be useful in pointing out certain absolute essentials. Many complicated procedures necessary to the special investigator are valueless to the practical clinician.

In the first place, a careful anamnesis should include in the past history questions as to: 1. Etiology—scarlet fever, sore throat, lead or mercury poisoning, evidence of protein sensitivity or asthma, this latter because of Longcope's demonstration that experimental renal disease may be produced by continued injections of foreign protein. 2. Dyspnea on exertion, for its contribution to cardiac insufficiency. 3. Previous attacks of edema, or urinary disturbances, such as hematuria. 4. Previous urinary examinations, this an attempt to delimit the duration of the disease.

The present illness should point out if possible: 1. A precipitating factor, such as acute infection or exposure to physical agents. 2. Headaches, if of the morning type so often seen in this disease. 3. Edema, its mode of onset and distribution. 4. Visual disturbances (easily confirmed by ophthalmoscopic examination). 5. Uremic manifestations, such as nausea, vomit-

ing, drowsiness, coma, twitching, or convulsions, are of very serious import. 6. Urinary abnormalities: (*a*) Polyuria may mean loss of concentrating ability; (*b*) Oliguria, suggesting salt retention, if accompanying edema; (*c*) Hematuria, very strongly implying a real inflammatory process in the kidney. 7. Dyspnea; this may be cardiac, may be due to hydrothorax as part of an anasarca, in some cases acidosis, or, finally, the type known as Cheyne-Stokes.

The history, in the main, makes two contributions: first and most important, the demonstration of unfavorable symptoms; and second, some idea as to the duration of the disease. I am purposely omitting nocturia because it is an unreliable symptom, influenced by many extraneous factors, and is, after all, entirely overruled by a study of the concentrating ability of the kidney. Obviously a full history along other lines should be taken; the points I have mentioned are those never to be omitted in the examination of a patient suspected of renal disease.

Physical examination may show no abnormality other than edema, this is the simplest and most hopeful case; but other patients have various abnormalities that indicate, in more or less degree, a severer disease. Certain of these findings when present in renal disease are almost invariably serious, while others merely add to the list of bad signs. Of the first type are: 1. Uremic manifestations—twitchings, coma, convulsions. 2. Cheyne-Stokes breathing. 3. Marked hypertension, 200 mm. systolic and over. 4. Acidosis, as demonstrated by Kussmahl breathing. 5. Retinitis.

The following are to be considered on the serious side, although not so consistently grave: 1. Emaciation. 2. Enlarged heart. 3. Anemia. 4. Thickened arteries. A red blood-cell and hemoglobin estimation should always be done, for the observation of anemia in the mucous membranes is often very deceptive. The number and degree of these physical findings present in a given case is the most valuable criterion of the severity of that patient's disease; entire absence of both groups with only edema present is the picture in pure salt retention; any of the first group with or without edema means nitrogen retention in

almost every instance. But a suggestive picture on physical examination should never permit omission of the functional studies.

The clinical examination of the urine should include: 1. Careful measuring of the total daily output. Polyuria with a constant weight on a controlled intake may be an evidence that concentration is poor. Oliguria may be a very serious sign if nitrogen retention is present. 2. Specific gravity. Frequent observations under a variety of conditions, being very careful that the instrument used is accurate; the significance I shall discuss later. 3. Microscopic examination for blood, or, more significant, red blood-cell casts. The value of this observation is the light it throws upon the presence of a complicating inflammatory process. An occasional red cell is usually insignificant. 4. Albumin and casts are the least interesting findings when the presence of renal disease is once established. Much albumin may be found in the mildest cases, sometimes none in the most severe. A quantitative estimation of albumin is worthless for the clinician, even if the inaccuracies of the clinical methods for its determination were less gross.

Our fundamental knowledge of renal function is sadly deficient. We can say objectively that the kidney performs a number of necessary services for the human body. The mechanism of these things is still largely hypothetic. In fact, in some instances, we really do not know whether the kidney is an active or a passive agent. Most distressing of all is the poor co-ordination of what physiologic and anatomic facts we have at our disposal. It is clear, therefore, that a study of renal function is necessarily superficial. But much valuable clinical material may be gleaned by a few simple procedures. First of all, it is necessary to understand the various functions and the significance of each.

The important functions include the following: 1. The excretion of water; many factors influence water output; among them are fluid intake, temperature and humidity of outside air, exercise, water excretion by bowel. The use of water as a vehicle of excretion is very essential, for, as Cushny points out, there are

over forty-six urinary constituents soluble in water, few of which are soluble in anything else.

2. The excretion of sodium chlorid: the amount is dependent largely on the intake, and the kidney so acts as to maintain a fairly constant level of chlorids in the blood. In this way the kidney is considered to be an important factor in preserving the necessary osmotic pressure of body fluids.

3. The excretion of certain substances aids in maintaining the neutrality of body fluids: (*a*) Acid phosphates are concentrated thirty times more in urine than in blood, a process of obvious value in getting rid of acid substances in the blood. (*b*) Ammonia is excreted as a salt combined with undesirable acid radicals. (*c*) Beta-oxybutyric acid is over two hundred times as concentrated in urine as in blood. It is clear that a marked decrease in these functions would produce a degree of acidosis that the respiratory mechanism would not be able successfully to combat.

4. The excretion of waste-products, largely nitrogenous, such as urea, creatinin, uric acid. These subatances are excreted normally as long as they are present in the blood. There is no attempt to preserve a constant level as in sodium chlorid.

5. The excretion of foreign substances, such as poisons or dyes.

6. The concentrating ability of the kidney should not logically be discussed with the preceding functions. It is a method of work, not a result accomplished, but I have mentioned it here because a clinical summary of the renal function in any given case includes it with the others. This function is a necessary safeguard to insure proper elimination when only small amounts of water are available to the kidney.

Having in mind the rationale of the kidney's various activities, we next must learn their practical application to clinical material, and we may consider them in the same order, which, however, is not an order of importance:

1. Water excretion, because of the many factors influencing renal water output, may be accurately studied only by constant observations of the body weight; an increase in weight meaning in general a holding up of fluids; a decrease, the reverse. Fre-

quent weighing of an edematous patient is absolutely essential if the patient is well enough to permit.

2. Salt excretion may be determined by a very simple clinical examination of the urine. The materials for this test are inexpensive, the technic easy; there is no excuse for its omission by any practitioner. The specific holding up of salt in the uncomplicated edematous type represents often an excretion of less than 1 gm. a day, while, although the more severe types without edema rarely excrete normal amounts, they seldom go below 1 gm. Of course, it must never be forgotten that the salt intake influences excretion markedly. During diuresis the salt output increases, and a relapse may often be predicted by a rapidly decreasing output of salt.

3. Evidences of acidosis, clinical and chemical, are proof of the decrease in this function, but the clinical value is slight because this condition always occurs in the very latest stage of the disease.

4. An impairment of the ability of the kidney to excrete nitrogenous waste-products is best studied by observing their accumulation in the blood. The simplest and most consistently satisfactory method is a determination of the amount of urea in the blood. Any man who has Wasserman reactions done on his patients can have this determination; drawing 10 c.c. of blood into a test-tube and sending it to the nearest chemical laboratory is all that is required to obtain this most valuable bit of information. No case of renal disease should be treated without at least one blood-urea determination. It is hard to give arbitrary figures on the upper level of normal. In general, on an average diet, an amount above 0.4 gm. per liter of urea is suspicious of impaired function, and the blood urea should be watched carefully; if it drops rapidly, it is, of course, less serious than if it remains constantly high. Nitrogen retention is a serious finding, it makes prognosis considerably worse; it is invaluable in its suggestions for treatment; in short, it changes one's point of view entirely.

5. Study of phenolsuphonephthalein excretion is the clinical application of this function of the kidney. The test has no bear-

ing on any particular one of the other functions, nor is it the quantitative test that its percentage expression would indicate. In the summing up of a case it should play a secondary rôle, for example, a very low phthalein is one more bad sign in a severe case, but a figure of 30, when uremia, hypertension, and nitrogen retention are present, is deceptive. In other words, if the phthalein stands out as a single incompatible factor in the total picture, it should be discounted. In surgical conditions this test plays a much more important rôle.

6. Studies of the concentrating ability over a twenty-four-hour period by the so-called renal test meal are inconclusive unless they give positive evidence that the kidney can concentrate, for too many factors may influence water excretion during such a short time. Two observations of a high specific gravity are worth very much more than a dozen never going above 1010. A very low water intake is the ideal method of testing this function, but the greatest fixation at a low level occurs when nitrogen retention is present, which is a contraindication to restricted fluid. When conclusively demonstrated, an inability to concentrate indicates considerable involvement of the kidney. The relative importance of abnormalities in this function may be compared with the phthalein excretion; alone they are of less significance than when fitting into and confirming the rest of the picture.

One of the most essential as well as the most difficult tasks is the exclusion of extrarenal factors or their proper balancing with the renal, when they are present. Predominant among these factors is the cardiac. Each case should be carefully observed for evidences of cardiac insufficiency, and it should be remembered that passive congestion of the kidney may exaggerate a comparatively mild impairment of renal function. Many cases of cardiac insufficiency with hypertension are called chronic nephritis when there are no findings distinctively associated with renal disease (for hypertension is more frequently found in other circumstances), and when the very slight impairment of function first observed disappears as the heart compensates. There are many cases, however, where it is practically impossible to disentangle the various factors.

Prognosis.—As this discussion has progressed the relative importance of certain evidences of grave import has been pointed out in the history, physical examination, and functional findings. The prognosis depends on the presence or absence of these factors. A patient whose history consists solely of edema, whose physical examination shows no other abnormality than edema, whose renal function is intact except for a specific inability to excrete salt and water—this patient has the best possible prognosis; he may live for years and be economically unaffected by his disease. Although, in any case of renal disease, the prognosis should be guarded, for the vagaries of the disease show themselves when least expected. Hematuria is significant because of its suggestion that an actual inflammatory process is present. The simple salt retention case I have just described may have present one or more of the serious findings in any and all combinations, and the edema itself may be absent. In any event, a prognostic analysis of the case means a gathering together of the grave signs, weighing their relative importance, and giving a common-sense opinion for the particular case at hand. In no disease is prognosis more difficult, but certainly more consistent correctness of prediction is possible with the point of view just described.

Treatment.—An analysis of each case suggests the most rational treatment for that case, certain general principles obtaining:

1. Rest in bed is indicated: (*a*) when edema is present, and should be continued for at least a week after its disappearance; (*b*) when hematuria is present, or (*c*) when the patient is too sick to be up.

2. Fluid intake should be limited to 1200 c.c. or below when there is retention of water as evidenced by edema. But if nitrogen is being retained, water must be given in larger amounts, at least 1800 c.c. if edema is present, and up to 2500 or 3000 c.c. if there be no edema. Inability to concentrate is a special indication for forcing fluids, because it means that the kidney requires much more water to excrete a given quantity of solids. If in the uncomplicated edematous cases limiting of fluid is unsuc-

cessful in producing a diuresis, forcing of fluids may, oddly enough, turn the tide in an occasional case.

3. The diet should always contain sufficient calories, there is never need for a starvation diet such as the Karrell; moreover, an attractive diet is quite as possible as an unattractive. For instance, use may be made of a large number of neutral vegetables containing no harmful substances; non-nitrogenous fruits are also available. Sodium chlorid must be markedly restricted in the edematous cases that are holding up chlorids, and decreased in all cases empirically. This may be accomplished for practical purposes by the omission of salt when food is being prepared, by the use of fresh butter, and the avoiding of essentially salty foods, such as salt fish. Nitrogenous food materials, the proteins, are given in proportion to the ease with which they are handled by the kidney; if there is no increase in blood urea they may form a normal proportion of the diet, but a high blood urea means restriction of protein to about 35 gm. a day. It must not be overlooked that eggs, fish, fowl, or beans are just as important as the so-called "red meats" when proteins are being considered. A patient who has once shown nitrogen retention should never be given more than 60 to 70 gm. of protein a day. It is very helpful to follow the influence of a low protein diet on the amount of urea retained in the blood.

4. Drugs specifically irritative to the kidney, such as mercury, should not be used. Saline catharsis is worth trying in edema. There is no contraindication to the use of iron in the anemic case not at death's door. Diuretics have long been a bone of contention. Our present status is as follows: There is definite evidence, experimentally and clinically (Christian), that diuretics are usually not effective in renal edema, and may, indeed, be harmful, particularly if real inflammation of the kidneys be present. One should, therefore, never use theocin or diuretin until he has been unsuccessful with all other means over a period of at least three weeks. At the end of that time one course may be tried, and occasionally real success will attend the administration, but if no results are obtained, do not repeat the drug. Diuretics are not indicated in any case without edema.

5. Bleeding is a procedure of doubtful value in any case—both theoretically and practically—if, however, it is done on an anemic patient it is worse than useless. It is one of those therapeutic procedures of more value to the onlooker than to the patient.

6. Hot packs may be used in the edematous cases when there is no nitrogen retention; if, however, the nitrogen excretion be impaired, they are contraindicated. If the pack be successful and a large amount of fluid is excreted by the skin, that much less fluid is available to the kidney as a vehicle for the excretion of waste products, whose excretion by the skin is far less efficient than by the kidneys. It is possible to precipitate an attack of uremia in the nitrogen retention type of case by the use of hot packs.

7. In those cases where the prognosis is good, typically the salt retention type, a careful search for foci of infection should be made, and such as may be found removed. Tonsils and teeth are by far the most frequently found abnormalities.

Therapy is very discouraging because we can make no attack on the cause of the disease or diseases—for it is as yet unknown. All of the general principles I have mentioned are possible of exception. An open mind is absolutely necessary to a proper understanding and treatment of renal disease—the explosion of one's pet theories is inevitable if one continues to see cases. An attempt at rational analysis and treatment based on the few well-established facts at our disposal, should be our aim.

In conclusion I wish to present 3 cases:

CASE I.—Man, aet. twenty-seven years, admitted to the hospital complaining of swelling of his legs and ankles for two days.

Family History.—Mother died at fifty-two of kidney trouble.

Past History.—Hives at fifteen years; otherwise entirely negative.

Present Illness.—Slight cough for one week; frontal headache three days ago; two days ago noticed that his feet were swollen; no other symptoms.

Physical Examination.—Marked general edema; severe pyor-

rhea; heart slightly enlarged at left. B.-p. 154/90; eye-grounds negative.

Blood.—R. B. C. = 3,570,000. Hb. = 70 per cent.

Urine.—Amount; started diuresis immediately. Sp. gravity; 1033 in one specimen. Albumin, very faint trace; Micro., few casts and occasional r. b. c.

Function.—1. Water excretion good, because of diuresis. 2. Salt excretion not decreased, because of diuresis. 3. Blood urea = 0.38 gm. p. l. 4. Phthalein = 44. 4. Concentrating ability to 1033.

Course.—Diuresis began before any observation was possible; edema rapidly disappeared. B.-p. fell to normal and patient was discharged in two months, quite well.

Discussion.—A case of salt retention type, with some anemia and a slightly enlarged heart as the only signs of severity. These are less important ones, and functional studies show no urea retention. We could therefore predict a good outcome. Treatment may neglect the protein factor.

CASE II.—Man, aet. forty-two, admitted to the hospital complaining of dimness of vision for five weeks.

Family History.—Negative.

Past History.—Always healthy; rejected for life insurance because of albuminuria four years previous. Gonorrhea five years ago.

Present Illness.—Failing vision for five weeks accompanied by some dyspnea on exertion, and an occasional headache. No other symptoms. Comes to hospital at advice of oculist.

Physical Examination.—Well nourished, no edema, mucous membranes pale; heart enlarged considerably to left. B.-p., 210/145; eye-grounds show definite edema of the disks.

Blood.—R. b. c. = 4,000,000. Hb. = 50 per cent.

Urine.—Amount; 1000 c.c., decreasing later. Sp. gravity; 1014, 1014, 1010, 1010. Albumin; heavy trace. Micro.; no r. b. c.; many casts.

Function.—1. Water excretion; no edema; fair excretion at first, but decreased later. 2. Salt excretion 5 gm. a day; decreased, but not specifically held up. 3. Blood CO_2, 21 mm. of

Hg.; definite acidosis. 4. Blood urea = 3.31 gm. per liter, a marked retention. 5. Phthalein = 0. 6. No positive evidence either way as to the concentrating ability of the kidney, but no high specific gravity observed.

Course.—Progressively down hill, with death ensuing in one month.

Discussion.—An apparently well man, whose history and physical examination showed two very grave signs—retinitis and marked hypertension—plus anemia and an enlarged heart; we would expect serious impairment of renal function, and, indeed, the urea is very high, phthalein very low, and an acidosis is present. All the findings agree on severe disease, and the course justifies that conclusion. Treatment was too late to be effective.

CASE III.—Man, aet. twenty-six, admitted to the hospital complaining of swelling of the face for ten days. Family history negative.

Past History.—Has worked as a compositor for eight years, but has never had any symptoms of lead-poisoning. Bell's palsy eight years ago. No cardiac or renal symptoms.

Present Illness.—Slight cough twelve or thirteen days ago. Swelling of face ten days ago, extending rapidly to whole body. No other symptoms.

Physical Examination.—A general edema; carious teeth; large tonsils; heart enlarged to left; B.-p. 178/112; eye-grounds negative.

Blood.—R. b. c. = 4,350,000. Hb. = 79 per cent. Smear = no stippling of red cells.

Urine.—Amount consistently low—300 to 600 c.c. Sp. gravity; 1017. Albumin; very heavy trace. Micro.; hyaline casts; few r. b. c.; no lead.

Function.—1. Water excretion very poor; increasing weight and edema. 2. Salt excretion less than 0.5 gm. a day. 3. Blood CO_2 = 24.8 mm. Hg., acidosis. 4. Blood urea = 1.56 gm. per liter. 5. Phthalein = 20. 6. No evidence on concentrating ability.

Course.—The patient continued to retain salt and water. His blood urea went up and his phthalein excretion decreased. In two months he had become uremic, and died shortly afterward.

Discussion.—The history suggested simple salt retention. The physical examination offered no real evidence against this possibility except that the blood-pressure was higher than one expects to find. Functional study showed a specific holding up of salt and water, and the phthalein excretion was not tremendously low—in other words, without a blood urea we would have given a good prognosis, treated him as Case I was treated, with restricted fluids; in short, been led quite astray. But the nitrogen retention immediately modifies our prognosis and our treatment. The course justifies the prognosis, if not the treatment.

CLINIC OF DR. EUGENE F. DuBOIS

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THE BASAL METABOLISM AS A GUIDE IN THE DIAGNOSIS AND TREATMENT OF THYROID DISEASE[1]

It is an easy matter to make a diagnosis in a typical case of hyperthyroidism presenting the cardinal symptoms of goiter, exophthalmos, tremor, and rapid pulse. Even a layman can tell what the trouble is at a glance if he has ever had a friend with Graves' disease. Typical cretinism can be diagnosed by anyone who has traveled in the Alps. In marked contrast to these extremes there is a large group in which it is most difficult to decide whether or not the patient is suffering from increased or decreased activity of the thyroid gland. These are the very cases in which a correct diagnosis is most important because of the good results that can be obtained by proper treatment.

Scores of tests have been presented as an aid in confirming the diagnosis of exophthalmic goiter. There is only one that stands out as a rational measure of the degree of hyperthyroidism, and that is the measurement of the basal metabolism. Since this is a matter of some complexity it may be well to discuss it before presenting the individual patients studied by this method.

The basal metabolism of a man is represented by the number of calories he produces in the morning hours, before breakfast while resting quietly in bed. Usually this is expressed in terms of calories per hour per square meter of body surface. The study of a large number of normal men and women has shown that the level of the basal metabolism varies with the age, sex,

[1] A series of cases in the metabolism ward of the Russell Sage Institute of Pathology in Bellevue Hospital presented to the students of Cornell University Medical College.

and surface area of the individual. Just why the metabolism should be proportional to the surface area is not clear, but the fact seems well established and is of great convenience in expressing the normal standards. Once having determined a man's heat production and having estimated his surface area from his height and weight, it is easy to compare the result with the normal standard for his age and state that his basal metabolism is such and such a percentage above or below the normal average. There are comparatively few normal individuals whose basal figures are more than 10 per cent. above or below the average. Practically all come within the 15 per cent. limit.[1]

A few years ago the measurement of the heat production was a difficult matter, attempted in only a few laboratories and clinics. At the present time there are half a dozen hospitals in this country where these tests are being made, especially on patients with exophthalmic goiter. In most places one of the simpler forms of apparatus is used, such as the Benedict universal respiration apparatus or the Tissot spirometer.[2] These measure the oxygen consumption in periods of ten to fifteen minutes, allowing one to calculate the heat production by the method of indirect calorimetry. Much more complicated is the large respiration calorimeter, such as was used in the study of the patients here presented.

As might be expected, there are several diseases which cause an increase in the basal metabolism. Patients with high fever

[1] Lusk, The Elements of the Science of Nutrition, 3d ed., Phila., 1917, W. B. Saunders Co.

Gephart, F. C., and DuBois, E. F., Clinical Calorimetry, Paper IV, The Determination of the Basal Metabolism and the Effect of Food, Arch. Int. Med., 1915, xv, 835.

DuBois, D., and DuBois, E. F., Clin. Cal., Paper X, A Formula to Estimate the Approximate Surface Area if Height and Weight be Known, Ibid., 1916, xvii, 863.

Aub, J. C., and DuBois, E. F., Clin. Cal., Paper XIX, The Basal Metabolism of Old Men, Ibid., 1917, xix, 823.

[2] Carpenter, T. M., A Comparison of Methods for Determining the Respiratory Exchange of Man, Carnegie Institution of Washington, Publication No. 216, Washington, 1915.

Benedict, F. G., A Portable Respiration Apparatus for Clinical Use, Boston Med. and Surg. Jour., 1918, clxxviii, 667.

are 30 to 40 per cent. higher than normal. In severe cardiac and renal disease and anemia the results may be high, and in leukemias with very large numbers of white cells the heat production may be almost double the normal. Some patients with acromegaly give high results.

Fortunately, most of these conditions are easily diagnosed and are seldom confused with thyroid disease. It is in hyperthyroidism that we find the highest basal metabolism, and there is a striking parallelism between the severity of the disease and the level of the heat production. In very severe cases the increase is more than 75 per cent., in severe cases 50 to 75 per cent., and in moderately severe and mild cases less than 50 per cent. Conversely, in cretinism and myxedema the metabolism may be 20 to 40 per cent. below the normal average, figures lower than in any other condition except profound emaciation. In such cases of deficient thyroid secretion the metabolism can be raised by the proper administration of thyroid extract.

An increased basal metabolism is not pathognomonic of hyperthyroidism any more than sugar in the urine is pathognomonic of diabetes. In fact, there is a striking similarity between these leading manifestations of the two great diseases of metabolism—diabetes and hyperthyroidism. If a patient complains of polyuria, polydipsia, and loss of weight and strength in spite of an increased appetite, we suspect that there is some interference with the oxidation of the carbohydrates, and confirm the diagnosis by testing the urine for sugar. If another patient gives a history of mental irritability, rapid, throbbing heart action, warm, sweating skin, increased appetite, and loss of weight we recognize that these are the symptoms of increased metabolism, and if fortunate enough to have the means at our disposal we confirm the diagnosis of hyperthyroidism by measuring the heat production. In this manner it may be possible to diagnose "exophthalmic goiter" without waiting for the appearance of exophthalmos or goiter. In diabetes we gage the effect of treatment by determining how much carbohydrate can be oxidized. In hyperthyroidism we can follow the course of the disease by watching the fluctuations in the basal metabolism.

The first patient is Anna K.,[1] referred to the metabolism ward by Dr. John Rogers. She is a nurse, twenty-six years old, of a rather neurotic family. At the age of sixteen she had rheumatic fever, and since then has been high strung and easily frightened. For several years she has suffered from dyspnea and palpitation on exertion, and about a year and a half ago these symptoms grew worse, and she began to have severe headaches, marked sweating of the skin, excessive appetite, and thirst. Two months ago she was badly frightened in a runaway and all the symptoms increased in severity. Since then she has been taking a special thyroid "residue" prepared at the Loomis Laboratory. On April 4th both superior thyroid arteries were ligated by Dr. Rogers in this hospital.

On April 28th, at the time of the first calorimeter observation, she presented the picture of extreme hyperthyroidism except that there was only slight exophthalmos and no lagging of the lids on looking downward. The expression was tired and neurotic, the eyelids were puffy, and the voice weak. The frame was small and she was very thin, weighing only 98 pounds, which was 15 less than her usual weight. The thyroid gland was moderately enlarged, especially on the right side. The tongue and hands were tremulous, the skin moist and warm. The cardiac impulse was diffuse, maximum in the fifth space, 8.5 cm. to the left of the midline. The action was regular, averaging 121 per minute.

The first hour that she was in the respiration calorimeter she produced 102.6 calories; the second hour, 101.5. According to her surface area this was 104 per cent. above the normal average. This means that every square inch of her skin was giving off twice as much heat as in the case of a normal woman, so it is no wonder that it felt warm and moist. Her food requirement was double the normal, and her emaciation showed that the intake had not increased correspondingly.

On April 29th, the day after this observation, Dr. Rogers

[1] The details of histories and laboratory findings have been published in Clinical Calorimetry, 14th Paper, Metabolism in Exophthalmic Goiter, Arch. Int. Med., 1916, xvii, 915.

ligated the two inferior thyroid arteries. She stood the operation well, and on May 13th returned for another test in the calorimeter, feeling less nervous and more ambitious. This time she produced an average of 84.2 calories per hour, which was 71 per cent. above the normal average for a woman of her weight. The pulse-rate had fallen to 100 per minute.

This case illustrates several points. It shows that there can be an extreme degree of hyperthyroidism with only slight exophthalmos and moderate enlargement of the thyroid. It indicates an improvement following ligation of the arteries, but demonstrates that the gland can be markedly overactive even though all four thyroid arteries have been tied.

The second patient, Benny London, is at the other end of the scale of thyroid activity. He is a cretin of the type that used to be so common in some of the villages of Switzerland and Northern Italy. He has been at the Children's Hospital on Randall's Island for the last twenty years, and it is believed that he is about thirty-six years old. His mental and physical development corresponds to that of a small boy of seven. After twenty years of schooling he has finally learned how to write his name. Attempts to transplant sheep's thyroid into the abdominal wall and pelvis of the kidney failed to produce any beneficial results, and apparently caused the formation of a renal calculus. He has had numerous courses of treatment with Parke, Davis & Co. thyroid extract, but on doses as small as ½ to 1 grain three times a day develops tachycardia, weakness, and often syncope.

Benny is only 3 feet, 7½ inches tall and he weighs 51 pounds. His face is broad, eyelids baggy, lips thick, nose broad, teeth widely spaced. No thyroid gland can be felt. There is a small umbilical hernia and there are pads of fat on either side of the neck and others just anterior to the axillæ. His genitals resemble those of a boy of seven and there are no male secondary sexual characteristics. The skin is very dry, harsh, inelastic, with fine branny desquamation. His Wassermann test is strongly positive, the urine contains much sterile pus, apparently due to the calculi in the pelves of the kidneys. The temperature is slightly subnormal and the pulse 64 to 80.

Two calorimeter observations thirteen days apart show a basal metabolism 17 and 22 per cent. below the normal adult figure as based on his surface area. This means that he produces about half as much heat as a normal seven-year-old boy of his size because normal children show a very high basal metabolism.

After three days of treatment with thyroid extract, 3 grains a day, his metabolism returned almost exactly to the normal average for adults, but the temperature rose to 100° F., pulse to 100, and he felt so limp and looked so miserable that it was necessary to discontinue the extract.

No more popular patient has ever been in the ward than this little cretin. He is docile, uniformly good natured, full of fun, and blessed with a most contagious grin. At first his favorite occupation was hunting for bugs with a flash light, but he was disappointed by the negative results in Bellevue Hospital. He is a natural clown, and his humor is of a type that might well have been popular with the medieval monarchs who used these cretins as court jesters.

Our third patient, Max W., has been most unpopular in the ward because he teases his neighbors—the cretin and a pituitary patient of slow mentality. His excitable disposition and quick thoughts and actions show the driving force of too much thyroid secretion.

Max is a Rumanian Hebrew, forty years old, and for some time has been a storekeeper in this city. Two years before he came to the hospital he was refused life insurance because he weighed 190 pounds. A year before his first calorimeter observation he received news that his brother had been murdered and was much excited for a week. The next month he began to suffer from nervousness, loss of weight, and a severe, unproductive cough. He was sent to the mountains with a diagnosis of tuberculosis, but did not improve. It was then found that his Wassermann reaction was positive, and he was treated with mercury, still without improvement. Next he went to Mount Sinai Hospital, where they made a diagnosis of exophthalmic goiter and started medical treatment. He was discharged from this and one other hospital on account of quarrels with the nurses and

staff. He vehemently refuses surgical treatment because he saw a patient die after a thyroid operation. On the whole, he seems to have a poor opinion of the medical profession.

The patient is tall, but weighs only 136 pounds. His skin is warm and slightly cyanotic. The expression is angry and the eyes are staring, with slight protrusion. Although the upper lid covers about 2 mm. of the cornea, it does not follow the eyeball when he looks downward. There is some weakness of convergence; he winks but seldom, and the forehead wrinkles but slightly. His thyroid gland is soft and moderately enlarged, especially the right lobe. When admitted to Bellevue the cardiac apex was in the fifth space, 11 cm. to the left of the midline, and the action was rapid, 108 to 142, with a marked irregularity of the respiratory type. At the apex was a soft systolic murmur. The urine showed traces of sugar and the Wassermann was strongly positive.

On Feb. 16th, five days after admission to the hospital, his basal metabolism was 75 per cent. above the average normal. Four days later it dropped to 60 per cent., but after a week rose to 65 per cent. above the average. On March 4th it had fallen again to 54 per cent. This shows the improvement that follows rest in bed without medication. After March 5th he was treated by Dr. Beebe, who gave him cytotoxic serum. The patient felt much better and did not even object to the local reactions, which at times were severe. The metabolism fell slightly, reaching 39 to 53 per cent. above the normal. A year later he returned to the ward, saying that he was much stronger and less excitable. He had gained 22 pounds in weight and had been able to work in his store. The goiter was a little smaller, the eye symptoms were unchanged, and the skin was still moist and warm. The heart was fibrillating and the apex was 13.3 cm. to the left of the midline. His metabolism was 45 per cent. above the average.

It has been stated that this patient's urine contained traces of sugar. He was by no means a diabetic, as is shown by the fact that his blood-sugar remained normal on a diet containing 200 to 300 grams of carbohydrate. Absolute proof of his ability to oxidize sugar was furnished by the calorimeter. After taking 100

grams of glucose his respiratory quotients showed that he was deriving 60 to 90 per cent. of his calories from carbohydrate combustion.

This case illustrates that a patient suffering from hyperthyroidism can have his troubles ascribed first to tuberculosis and next to syphilis. If his doctor had examined his urine he might have been treated for diabetes also. The calorimeter indicated that rest in bed caused his basal metabolism to fall from 75 per cent. above the normal average to 54 per cent. A year's treatment with serum was not able to cause a drop of more than 9 per cent.

Our fourth patient, Anna R., has been followed for two years. She was the first thyroid patient tested in the calorimeter. When first seen she was twenty-nine years old, unmarried, a saleswoman. Five years before this she had typhoid fever, and on recovery noticed a swelling of her neck. Since then she has suffered from tremor, palpitation, restlessness, and loss of weight, but has been able to work up to the time of admission. She thinks she has improved during the last two years, but says that her friends noticed that her eyes were staring about one year ago.

The patient is tall and thin, with distinct exophthalmos and von Graefe's and Stellwag's signs. The thyroid is moderately enlarged, there is a slight tremor of the tongue and hands. The heart is slightly enlarged, the pulse 84 to 88.

On May 10th her basal metabolism was 34 per cent. above the normal average. On May 12th, under local anesthesia, the left superior and right inferior thyroid arteries were ligated and the tip of the left upper pole removed. On the 16th the other two thyroid arteries were ligated and the right upper pole removed. For fear that she might suffer from a sudden diminution of thyroid secretion she was given ½ grain of thyroid extract every four hours until May 18th. On the 20th her metabolism was higher than before the operation, registering 55 per cent. above the average. Eight days later it was 52 per cent. This shows that an operation can increase the activity of the thyroid gland.

After leaving the hospital she spent a couple of months in the

country and gained weight and strength. She was then able to go back to work. A year after her operation she returned for a calorimeter observation. The thyroid was still enlarged, she was still weak and nervous, but her general condition was somewhat improved. Her basal metabolism was exactly the same as at the time of her first test.

A week later she was married and did well until her husband lost his job and she had to start work again in the store. When she reported at the metabolism ward two years after the first observation she was very thin, extremely nervous, and tremulous. Her skin was moist and the pulse small and weak. Unfortunately, it was not possible to measure her metabolism, but it was undoubtedly increased as a result of her efforts to support herself and her husband.

The fifth patient, Mrs. S., is in comfortable circumstances, but her breakdown was hastened by overwork, just as in the case of the saleswoman. She has always been energetic and athletic, but about five years ago developed an unusual degree of activity and restlessness. This led her to play tennis violently, and she won many cups in tournaments. She devoted herself to charities until it was evident that she was becoming nervous, irritable, and short of breath on exertion. A severe unproductive cough coupled with loss of weight made the family doctor suspect tuberculosis, and he sent her to a consultant. No diagnosis was made until the patient's mother-in-law suggested that the trouble was exophthalmic goiter, since the expression of the eyes reminded her of a man she knew who was suffering from this disease. A flood of light came to the family doctor, who promptly discovered a slight tremor, distinct tachycardia, puffiness of the eyelids, and unusual brilliancy in the eyes. On questioning, the patient admitted that she slept with very few blankets even on cold nights, and that her skin was always warm. In spite of treatment the condition grew worse and the exophthalmos became distinct, although there was never a goiterous swelling. Ligation of both superior thyroid arteries was performed by Dr. John Rogers, and during the next few years there was a slow improvement. The exophthalmos persisted, but the slight thick-

ening of the skin and some of the mental symptoms suggested that there was possibly an exhaustion of the gland with threatened myxedema. In order to see if thyroid extract were indicated Dr. Rogers advised a test to determine the level of the basal metabolism. The calorimeter showed that the heat production was 20 per cent. above the normal level and that the gland was still in the stage of hypersecretion.

The sixth and last patient, Peter N., was a puzzler. He was considered to be a case of atypical exophthalmic goiter and was referred to the metabolism ward to see if an operation were advisable. He was twenty-three years old and 6 feet 2 inches in height. His father was 6 feet 4 inches. The patient grew fast between the ages of fifteen and eighteen and became weak and nervous, losing his temper easily. He suffered from headaches two or three times a week, and about a year ago his hands grew so tremulous that he had to give up his work as mechanic. Shortly after this he went to the Massachusetts General Hospital, where his respiratory metabolism was studied by Dr. J. H. Means and found to be within normal limits. The superior thyroid arteries were ligated by the surgeons, and since then the headaches have been rather less frequent, but he is not much stronger and he only sleeps two or three hours at night.

The young man is tall and thin, but there is no suggestion of acromegaly in his appearance and the *x*-ray shows that the sella turcica is normal in contour. His expression is anxious, but there are no eye symptoms. The thyroid is soft and slightly enlarged. The hands and feet are sweating and there is marked dermatographia. Cardiac dulness extends 12 cm. to the left of the midline and the electrocardiogram shows a slight respiratory arhythmia. The pulse-rate is only 71. There is a trace of sugar in the urine.

One observation in the calorimeter showed that his metabolism was 2 per cent. below the average; in other words, absolutely normal. This, together with the test made a year previously by Dr. Means, rules out hyperthyroidism. In the light of our present knowledge we might suspect that this is a case of neurocirculatory asthenia.

As we review the preceding cases from the purely clinical aspect we are struck by the importance of symptoms outside the classical group of exophthalmos, goiter, tremor, and tachycardia. As Plummer has pointed out, the earliest symptoms are cerebral stimulation, vasomotor disturbances of the skin, tremor, mental irritability, tachycardia, and loss of strength. In two of the cases we have noted that there was an irritative cough, which led the physician to suspect tuberculosis. Before there is distinct exophthalmos there is usually a peculiar look of the eyes, an unusual brilliance, a slightly startled, angry expression. There is also an impulsiveness of manner and distinct restlessness of disposition. Often the patients complain that they cannot get along with people and especially with their own families.

Under ordinary conditions a man loses about three-quarters of the heat he produces by radiation and conduction from the surface of his body. About one-quarter is lost by the evaporation of water from skin and lungs. Therefore the increased heat production in hyperthyroidism manifests itself in a warm skin which breaks out into sweat on slight provocation. The patient even while at rest feels warm, just as if he were exercising. He needs but little covering at night. To supply all this extra heat it is necessary for him to eat large quantities of food.

We have seen that in the cases here presented the basal metabolism has been an acurate guide as to the degree of thyroid activity. The question naturally arises as to whether or not this holds good for all cases. Past experience has shown that there are few pathognomonic signs in medicine. Particularly in diseases of the ductless glands scores of tests have been discarded as worthless. It will take several hundred metabolism experiments with patients carefully standardized from the clinical viewpoint before one can say that the basal metabolism is an absolutely accurate guide in the diagnosis and treatment of thyroid disease. We can, however, at the present time say that it is the best guide, much safer than any other one sign or symptom. It is a better guide in doubtful cases than the opinion of nine out of ten consultants.

The test has a firm physiologic and pathologic basis. It is purely objective, and cannot be influenced by the hopes of the patient or his physician. Since the phenomenon was first discovered by Friedreich Müller in 1893 and confirmed two years later by Magnus-Levy, its significance has not been disputed, although it has been grossly ignored. In Germany the level of the metabolism has been used in a few experiments as a method of testing different forms of treatment. In this country, shortly before the war, a large number of observations were being made in various clinics. In recent publications by Means and Aub,[1] White and Aub,[2] and by Peabody, Wearn, and Tompkins[3] it seems to be accepted as a standard of thyroid activity. Peabody has shown that a large proportion of the cases referred to the Army General Hospital at Lakewood as hyperthyroidism were incorrectly diagnosed.

Granting the value of the test, is it practicable? Calorimeters are out of the question except in a few laboratories. On the other hand, the simpler forms of apparatus for determining the basal metabolism are comparatively reasonable in cost and fairly easy to operate. They are much less expensive than an electrocardiogram and the technic is not so difficult. Still there are many pitfalls waiting for the careless investigator, and it is advisable that any man who starts to measure the total metabolism should begin with a series of normal controls.

"But why," says the practitioner, "should I, who have seen hundreds of cases, go to all this trouble when I can perfectly well tell from the clinical aspect whether or not the metabolism is increased?" Such guessing is very common, quite fascinating, and not risky for one's reputation unless the results are checked. On the other hand, those clinicians who have checked up their guesses in two or three hundred experiments realize the fre-

[1] Means, J. H., and Aub, J. C., A Study of Exophthalmic Goiter from the Point of View of the Basal Metabolism, Jour. Amer. Med. Assoc., 1917, 69, 33.

[2] White, P. D., and Aub, J. C., The Electrocardiogram in Thyroid Disease, Arch. Int. Med., 1918, 22, 766.

[3] Peabody, F. W., Wearn, J. T., and Tompkins, Edna H., The Basal Metabolism in Cases of the "Irritable Heart of Soldiers," Medical Clinics of North America, September, 1918, U. S. Army Number.

quency of their errors, especially in atypical cases, and are not at all surprised if they do not come within 40 per cent. of the true figure.

The diagnostician who interprets the basal metabolism intelligently will be able to determine the degree of thyroid activity. The surgeon who operates on thyroid patients will find that the basal metabolism is of great help in following his results. He will also find that in many cases a fifteen-minute test with the respiration apparatus will save the patient a needless operation.

CLINIC OF DR. WILLY MEYER

LENOX HILL HOSPITAL

ADVANCED PULMONARY TUBERCULOSIS, A BORDERLAND DISEASE

Presentation of a Patient Operated Upon with Subsequent Results.

GENTLEMEN:

For many years it has been my pleasure to select from my personal practical experience, for presentation before you, cases which are types of the borderland diseases.

It is well known to you that in the course of the last decade many patients afflicted with all the well-known diseases of the gastro-intestinal tract, with its contributory adjacent glands, the liver and gall-bladder, and pancreas, as well as the spleen, no less than many affections of the central nervous system and urinary system, have become borderland cases. At any time they may pass from the domain of the medical man across the borderline into surgery. The "when" depends on the inclination of the attending physician, or one might perhaps better say on his "conservatism." There are still some of our colleagues, thoroughly educated and learned men, who abhor the entrance of the surgeon into their fields, who cling to their chemical and physical therapeutics to the very last, and often assign even the cancerous affections of the organs mentioned above to the surgeon for operation when it is too late. To my mind, the standing of the modern physician can and must be estimated by his mental and energetic grasp of what medical science calls "borderland" today, by his readiness and the timely call of his conscience to realize that in the given case his personal, no matter how careful,

attendance can be superseded by a scientific operator to the advantage of his client.

One of the latest chapters added to the borderland list is that of advanced pulmonary tuberculosis.

It is generally recognized today that artificial pneumothorax (Forlanini-Murphy) is of great assistance in the treatment of pulmonary tuberculosis. Carefully supervised treatment by the internist or specialist, in combination with proper hygienic measures, are the necessary additions. No doubt many patients suffering from tuberculosis of the lung get well under such treatment; others are so improved as to lead a satisfactory existence for many years.

But what, if adhesions have united the pulmonary to the costal pleura; if the needle again and again fails to find a place in which the nitrogen or pure air can be blown in successfully; if also all the other measures of scientific régime do not bring improvement? If no other treatment were at hand, or resorted to, all these patients would be doomed; they would surely die within a brief space of time.

It is in these patients and at this stage that modern operative surgery steps in.

I. BRAUER-FRIEDRICH METHOD

Friedrich, of Marburg, on the initiative of Brauer, then the internist of the same university, took up this question in 1908. They reasoned that the required collapse, compression, and artificially putting at rest of the diseased lung could be accomplished by attacking the skeleton of the chest, if the presence of far-reaching adhesions between the two pleural leaves prevented the nitrogen or air insufflation into the pleural sac. They argued that resection of the tenth to the second or first rib, inclusive, with subsequent artificial mechanical compression of the side of the chest from without must in such cases accomplish, in part at least, the same final result as the Forlanini-Murphy method was doing in more favorable cases with non-adherent pleuræ. Friedrich thereupon cut out the ribs mentioned after having gained the necessary access to the bony thoracic wall

by means of Schede's incision. The work was done in one sitting under a superficial morphin-chloroform anesthesia, and was termed "extrapleural thoracoplasty."

Friedrich addressed the American Surgical Association on this subject at its meeting in Philadelphia in June, 1909. In 1911 he was able to report on 28 patients. There were 8 deaths (28.5 per cent.) and 20 recoveries from the operation; of the latter, 16 were much improved, 3 improved, together = 68 per cent., and 1 not improved. All the patients had been desperately ill. Nevertheless 68 per cent., = two-thirds, were improved by the operation.

II. SAUERBRUCH'S METHOD

For weak and reduced individuals, as represented by the majority of these patients, the Brauer-Friedrich procedure represents a serious undertaking. Friedrich's genial first assistant, F. Sauerbruch, therefore tried to modify and simplify it by operating in stages and under regional plus local novacain-anesthesia. In order to avoid the threatening aspiration-pneumonia of the lower lobe from a purulent cavity in the upper lobe, he proposed, first resecting the tenth to sixth ribs inclusive and compressing the lung with a pad and elastic straps, and then, two or three weeks later, remove sufficiently large pieces of the fifth to the second or first ribs. He also showed that only the posterior half of Schede's incision is required for an exposure of a sufficient length of the ribs for resection (hook incision).

The latest results published by Sauerbruch in 1913 are remarkable. Of 113 patients treated with extrapleural thoracoplasty he operated upon 77 for advanced pulmonary tuberculosis. Of these, 17 were cured, 20 greatly improved, 19 improved, together 56 = three-quarters = 73.7 per cent.; 4 remained unchanged = 5.2 per cent.; 3 got worse = 4 per cent.; 2 died soon after the operation (2.6 per cent.); 11 died of tuberculosis later on (14.5 per cent.), together death-rate = 17.1 per cent. All the cases were carefully selected by specialists in tuberculosis, and the majority of them came down for the operation to the University Clinic at Zurich from Davos in Switzerland,

and returned to the higher altitude after the operative recovery. "Unilateral affection" was the watchword, though slight involvement of the opposite lung did not definitely exclude the patient from the operation. Recent or progressing tubercular affection of the other lung and tuberculosis of the gastro-intestinal tract with diarrhea were considered a contraindication.

Sauerbruch succeeded in doing the operation with his trained set of permanent assistants, from the first incision to finishing the last skin suture, in nineteen minutes, a brilliant illustration of the effect of "crew-work," as it was witnessed by members of the Southern Surgical Club who had gone to Zurich on their laid-out itinerary through the United States and Europe in the early summer of 1914.

Gradually an effort was made to do the resection of the tenth to the second rib in the same séance in stronger patients. If it was seen later on that additional compression of the lung was required to accomplish the desired result, the resection of the first rib from the front, also resection of the phrenic nerve at the neck (phrenicotomy) for permanent paralysation of the half of the diaphragm on the diseased side, and Tuffier's operation, "apicolysis," with insertion of a plombe of fat or paraffin, were added. The latter material was pushed into the space which had been artificially produced by separating the costal plus the adherent pulmonal pleura of the apex from the endothoracic fascia, and thus working down gradually, collapsing the apex. Resection of a short piece of the second or third rib in the preaxillary line with division of the posterior periosteal envelope of the rib started the operation and exposed the costal pleura.

The immediate result of this far-reaching mechanical collapse and compression of the lung is proliferation of connective tissue, gradual carnification of the lung, and reduction in size of former cavities. A pronounced chronic hyperemia sets in within the collapsed lung, according to Cloetta's careful investigations, which no doubt works in the sense of Bier's hyperemia, substituting the tuberculous infiltration with permanent scar tissue.

Hand in hand with this local organic improvement the

subsequent condition of the patient points to a steady change for the better. Cough with sputum becomes reduced or disappears, fever and night-sweats stop, tubercle bacilli can no longer be found, and the weight increases.

III. WILMS' METHOD

Wilms, of Heidelberg, did not fear the possible pneumonia in the lower lobe by aspiration, in consequence of multiple rib resection, in the presence of a cavity in the superior lobe. He favored the so-called "columnar resection" of the upper seven or nine ribs, anteriorly and posteriorly, in one sitting. The intermediate portion of the ribs left in place was used for more effective compression. He too worked under regional and local anesthesia. In 12 cases published there was no mortality.

All patients were much improved.

It is most interesting that the operative results of these three authors, who published the greatest series of such cases, are almost identical. All three succeeded in more or less arresting the disease in from 57 to 73 per cent. of their patients; that is to say, as many as 57 to 73 people out of 100 were either cured or much improved or improved. Certainly a remarkable record.

Personally, I have done the extrathoracic thoracoplasty seven times on advanced bronchiectasis in the course of the last ten years.

For this class of cases the operation represents one of the many so-called conservative operations which have been proposed for the surgical treatment of these unfortunates. It was the late Professor Friedrich, of Marburg, who persuaded me to proceed rather conservatively in the surgical treatment of patients suffering from advanced bronchiectasis, at the time of his visit to this country in 1909. He was of the opinion that every surgeon interested in thoracic surgery should make it his duty not to resort to lobectomy at once, but try less dangerous operations first. He feared that the youngest child of operative surgery, thoracic surgery, would not gain the confidence of our medical confrères and of the public if too many deaths were reported on the basis of too aggressive surgery. He there-

fore preached conservatism. Personally I followed him, and today look back on a series of conservative operations carried out on bronchiectatic patients, partially with regret and partially with satisfaction. With regret, because I failed to cure a number of advanced cases with bronchiectasis who might have had a better chance to live with properly performed lobectomy; and with satisfaction, because I succeeded with patience and perseverance in saving a few much-reduced patients from this terrible affliction who would most likely have succumbed to more radical work. There can be no doubt in my mind that exceptionally even somewhat advanced bronchiectatics can be *cured* by operations less serious than lobectomy.

At the present moment most careful individualization to establish the indications for operation is required in this class of cases. There can, however, be no discussion that in the advanced stage of bronchiectasis *only* the extirpation of the diseased lung lobe or lobes can bring permanent relief.

Looking back, a further source of satisfaction derived from my prolonged conservative operative work in this branch of surgery has been that I have made early acquaintance with extrapleural thorocoplasty under regional and local anesthesia. As stated before, I performed it seven times on these patients, a few times resecting the upper ribs from the tenth to the first inclusive, at one sitting, and conversed with the non-narcotized patient during the entire course of the operation.

Now, gentlemen, anybody might very properly ask me: How did it come about that this operation was performed on 7 cases of bronchiectasis and never before on a consumptive in the last ten years? The answer is that I was absolutely prevented from carrying out my intention to do so, in spite of frequent applications, by the board of directors of the various institutions with which I am connected. Not that these gentlemen were opposed to the operation, but because they were prevented from permitting the admission of patients with active tubercle bacilli in their sputum to our hospitals on the basis of an order of the proper health authorities. A patient with active tubercle bacilli in his sputum cannot be placed next to a patient suffer-

ing from a different disease in our public wards. In our private hospitals connected with the general hospitals it was rightly feared by the managers that the inmates would resent the presence of an advanced coughing and expectorating tubercular patient on the same floor. Thanks to the remarkable education of the public in matters tuberculous this certainly was to be feared.

In the case of the patient to be presented today, a thorough discussion of the subject before the house committee of the Lenox Hill Hospital resulted in permission to have such a case admitted to the isolation house. Fortunately, the courtesy of the superintendent permitted the use of an isolated room on the top floor of the main hospital.

The patient here before you, L. S., twenty-six years of age, was admitted to the Lenox Hill Hospital in November, 1918, having been sick with tuberculosis of the left lung since 1912. He had been residing since then, compiling chronologically, in Saranac Lake, Colorado, New Mexico, New York, and again in Saranac Lake. Tubercle bacilli were first found in 1914. The establishment of an artificial pneumothorax was impossible on account of wide adhesions, and he was sent to me by Dr. Baldwin and Dr. Trembley of Saranac Lake for operation.

The patient appeared very delicate, was short of breath on the slightest exertion, and had a rapid pulse. Every few weeks his temperature, following a slight chill, rose to 103° F. and more, and returned to normal gradually. The left lung showed clinically all the signs of far-reaching tuberculous infiltration with multiple cavity formation. The quantity of sputum equalled 60 c.c. in twenty-four hours. The right lung was but slightly affected.

It was decided to take the safest course and do, for the rib resection, a two-stage operation.

On November 18th the first stage was done, with regional and local novocain and adrenalin anesthesia. After infiltration of the desired line of incision the Kappis method was carried out first, 2 c.c. of the anesthetic solution ($\frac{1}{2}$ per cent. novocain) being deposited after striking the rib with a needle,

and 8 c.c. around the posterior branch of the thoracic nerves near the spine. Then the Schumacher method, also injection of novocain in weak percentage, was added, 5 c.c. of the same fluid being deposited at and below the angle of the tenth to the sixth left rib, 150 c.c. of the ½ per cent. in all were used. After some temporizing, during which time the patient was finally prepared for operation, the lower three-quarters of the typical posterior hook incision were painlessly carried out, the ribs sufficiently exposed after pulling the scapula aside and a piece of bone, 10 to 15 cm. long, from those ribs excised, well beyond the angle of the ribs. With two long split drainage-tubes in place, the wound was sutured in layers with a continuous stitch, and the dressing held in place by broad zinc adhesive plaster which also fixed the arm.

On the third day the first dressing was changed, when it was seen that the wound had healed by primary union. Two weeks later the patient was out of bed, improved in every respect. I made provision to begin at once with elastic compression by means of a pad, pulled by elastic straps to a loop surrounding shoulder- and hip-joint of the opposite side.

On December 5th, seventeen days after the first operation, it was considered wise to add the second stage, resection of the fifth to the second rib inclusive, again avoiding general anesthesia. Only a few drops of anesthol, more for quieting the patient's anxiety, were required once, for a short period. In order to expose a sufficient length of the upper ribs it became necessary, at the second stage, to incise the entire length of the first cut (Fig. 234), a rather pitiful procedure after primary union. The regret felt suggested trying to do the required resection in one stage if possible on somewhat preserved patients.

A flat cavity filled with serosanguinolent fluid was encountered near the spine. The latter evidently was aseptic, patient having had perfectly normal temperature continuously. The stumps of the ribs resected at the first operation were found to be covered with new, glistening, white connective tissue of remarkable thickness. Again drainage and dressing were applied as before. The patient was out of bed on the sixteenth

day. Compression with large and small pads day and night was arranged for.

Today the patient is greatly improved. His sputum is reduced and coughing spells are rare, the dyspnea is decreased;

Fig. 234.

he has gained in weight. The tubercle bacilli disappeared after the first operation and have never again been found up to date.

Through the courtesy of Dr. Baldwin, of Saranac Lake, the patient was allowed to return to that place. From there he writes to me under date of March 2d that he feels fine and strong and has full use of his left arm; his rectal temperature

has never trespassed 100° F., pulse is between 70 and 90 at rest and after exercise between 80 and 108; has had a severe coughing spell only on two days within six weeks; sputum is reduced one-half or more in quantity; he is able to walk many blocks without fatigue; his weight is gradually increasing.

Considering the fact that this patient was hopelessly lost without operation, his present condition is a source of continuous satisfaction.

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THE MEDICAL CLINICS
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VOLUME 2 NUMBER 5

CLINIC OF DR. HENRY A. CHRISTIAN

PETER BENT BRIGHAM HOSPITAL

CUTANEOUS PIGMENTATION, JAUNDICE, PALPABLE LIVER AND SPLEEN, AND ASCITES

December 9, 1918.

DR. CHRISTIAN: The patient (P. B. B. H., Med. No. 9841) that I wish to show this morning is a woman forty-four years of age, born in Ireland and having lived in Ireland until six years ago, when she came to Boston. She has lived in Boston since then. (To student who had been told to examine patient during demonstration of *x*-ray plates from another patient): Mr. ——, tell us in brief what you make out in this patient.

STUDENT: She has a rather dark skin, which she says is not particularly darker at present, she having always been rather dark, but perhaps not as dark as she is now. Her eyes are yellow, which is not due to pigmentation, but there seems to be fat over the scleræ.

DR. CHRISTIAN: Yes, there is a slight layer of fat which is yellowish, but, in addition, there is a slight general yellow color to the scleræ.

STUDENT: The mucous membrane seems normal. The hands are unpigmented. The chest and abdomen are a deep brown, with scars.

DR. CHRISTIAN: What did you say about her hands?

STUDENT: They are pretty white as contrasted with the face.

DR. CHRISTIAN: The face is definitely darker than the hands, but yet you can see, as contrasted to my hands and the hands

of the nurse, that there is also pigmentation of the hands, rather more about the forearms and elbows than in the hands, and the palms of the hands also show a slight degree of pigmentation. Pigmentation is more marked on the face than it is on the hands. It is more marked on the forearm than it is on the hand, and possibly it is increased a little bit in the upper arm as contrasted to the forearm.

You said the pigmentation was more marked on the abdomen than it was on the hand. What does the fact that the hands are less pigmented than the trunk suggest?

STUDENT: That it is not any form of pigmentation which depends on the action of sunlight for a deposition of the pigment.

DR. CHRISTIAN: Yes, there is some factor other than exposure to sunlight. If it were more marked on the face and hands, you would suspect exposure to the sun, but being less marked on the hands and distinctly more marked on the protected parts as well as on the face, which is unprotected, pretty well rules out pigmentation from exposure to sunlight. In the same way, it is always well in a case of pigmentation to see whether there is a sharp line of demarcation between the forehead and the adjacent scalp which is protected by the hair. In many cases there is often a definite difference in pigmentation at the hair-line between people exposed to the sun and those not so exposed, and particularly where they have worn hats do you get the change. Her scalp is pigmented, so she has this general pigmentation which, on the whole, is more marked on the face, neck, and thorax than it is on the hands. (Inspection of patient's feet.) There is not as marked pigmentation on the feet as on the face, but it is probably a little bit more marked on the feet than on the hands. While we are looking at her feet observe this distinct subcutaneous edema of the feet and of the lower leg.

What else did you make out in the brief time you had to examine her?

STUDENT: The abdomen is distended, apparently with fluid, because there is a fluid wave and dulness in both flanks and extending over the whole abdomen with the exception of a small area at the top, which is tympanitic.

DR. CHRISTIAN: The abdomen is distended, the greater part of the abdomen is dull, tympany is limited to a small area in the center, there is a fluid wave, and that is pretty good evidence of fluid. Did you feel the liver or spleen?

STUDENT: I could not get in; the abdomen is too tense.

DR. CHRISTIAN: The abdomen is tense, so that the liver and spleen were not made out. We cannot feel the liver and spleen when her abdomen is tense this way. She has been tapped, and after tapping the liver edge at times has been felt, not markedly enlarged, and the spleen has been felt, apparently the spleen, in a proportionate sense, being a little bit larger than the liver, but neither one is very large. The abdomen has not a uniform pigmentation, but there are pale areas where there is vitiligo or absent pigmentation, so she has this brownish pigmentation with areas showing absent or decreased pigmentation. There is a pale area on the abdomen about the size of a 5-cent piece, and there are smaller areas of that type scattered over the trunk, so we have a generalized pigmentation, brownish in color, more marked on the trunk than on the forearms or lower legs, present throughout the skin to a certain degree except in scattered small irregular areas, where there is an abnormal absence of pigmentation; we have a combination of cutaneous pigmentation and small areas of absent pigmentation or, as we call it, vitiligo. In addition, she has edema of the feet and ascites, and in the conjunctivæ a small trace of jaundice, not very marked; she has no evidence of jaundice as far as the skin goes.

Did you get a chance to examine her thorax?

STUDENT: I went over it hurriedly. The heart sounds below the nipple are very distant, and in the region of the second interspace there is a quite marked systolic murmur which is best heard there, but also is heard on the right side. The chest seemed normal on auscultation and on percussion in front. Behind, the sounds seem somewhat diminished on the left side.

DR. CHRISTIAN: Is that all over the lung or toward the base?

STUDENT: At the base, and, with the questionable dulness, the tactile fremitus seemed diminished at the same point.

DR. CHRISTIAN: That is quite characteristic. There is a

systolic murmur, but the heart is not enlarged. With that amount of fluid in the abdomen the heart naturally is encroached upon by the high diaphragm and somewhat disturbed in relation to the chest wall, so you do not get the maximum sounds where you might expect them. In the same way there are decreased breath sounds and dulness at the base behind, apparently a little more on one side; as far as we can judge, that is simply a high diaphragm crowded up against the heart in front, and, in the same way, on the lungs behind, giving a higher line of dulness than you ordinarily get, but the heart and lungs are essentially normal.

Since she has been in the hospital she has had a somewhat irregular fever, going at times fairly high. It is practically never normal throughout the twenty-four hours. Ordinarily it runs from a little below normal to about 100° F., with occasional higher elevations. When she first came in she ran a high temperature, at one time going up to 104° F., with a pulse a little fast—between 110 and 115. Recently her pulse has been running between 80 and 90. The respiration has been pretty uniformly between 20 and 25 for fourteen to fifteen days, and then it has run about 20 since, so from the chart there is no evidence of any disturbance in the cardiac or respiratory mechanism, but there is a slight irregular fever.

I will give you a little more about her history. There is no alcoholic history. She has been a person who has used a rather large amount of tea—six cups of tea daily. She has worked as an attendant nurse. Previous to five years ago she worked very hard, with long hours, but stood her work well. For many years she has been living with an elderly lady where the work has been very easy and congenial, she having her afternoons and evenings to herself. She had been doing this work up to the time of her admission. As I have already said, she was born in Ireland and lived there until six years ago.

There is no history of previous illness. As she expressed it, she was an unusually healthy woman. While living in Ireland she very frequently was closely associated with advanced cases of pulmonary tuberculosis, but gives no history of any symptoms

herself suggesting tuberculosis. There has been no disturbance in her head, eyes, or ears. In regard to her nose, she has had no discharge or any obstruction, but has had attacks of epistaxis during the past eight years associated, as she thinks, with her menstruation. Not every month, but almost six months out of the year she has a sudden nosebleed, mostly from the left nostril, just before the onset of her monthly sickness. She never loses more than 1 or 2 tablespoonfuls of blood at one time. These attacks of epistaxis ceased entirely two years ago until four months ago, when she had a single attack with her last menstrual period. She has had false teeth for two years. I do not know about her teeth prior to that. There is no cardiorespiratory disturbance in her past history.

The patient has always had a very good appetite and has eaten three heavy meals daily. Her bowels have always been regular without cathartics, averaging one or two movements daily. She has never felt nauseated or had gaseous eructations, although she has been troubled by gas per rectum at times, but this has not been present in the past four months. She never has had vomiting, hematemesis, distress, or colicky pains. Her color has always been dark, and frequently, since the age of twenty-eight, she says her skin has been dark and yellowish at intervals. So far as she knows her scleræ have never been yellow prior to the present illness. There is no history of diarrhea or clay-colored stools previous to the present illness. She gives a history of moderate smarting discomfort at stool suggesting the possibility of hemorrhoids. Prior to the present illness she had to get up from two to three times at night to pass her urine. During the past four or five months she has had no nocturia and thinks she has been passing smaller quantities of urine at a time. (Her chart confirms that since she has been in the hospital.) There has been no other abnormality noted in regard to her urine.

There is no history of any venereal disease and nothing to suggest a previous gonorrhea or syphilis. Previous to coming to the place at which she works at present her sleep was very irregular, but for the past three years she has slept very well.

There has been nothing abnormal about her history of sleep until quite recently, and I will bring that out in connection with the present illness. I presume the irregularity of sleep before that refers to her work as an attendant nurse, and that she had to get up from time to time in the course of her duties and so did not have regular sleep. The nurses abroad are rather apt to be on the job for twenty-four hours, and in taking care of a patient sleep in the room with the patient at night. They do not follow the American system of having a day and night nurse.

Her catamenia commenced at the age of fourteen and has always occurred with great regularity until four months ago, when she had her last period. She has always flowed abundantly, it lasting seven days. She has never suffered pain or had any symptoms during or after her periods. There was nothing abnormal about the catamenia except the associated nosebleeds already described. Her best weight was 141 pounds a month ago. Her average for the past ten years has been 140 pounds. She says she has been growing thin for at least two months, and all her friends remarked her loss of flesh, and yet she weighs as much as she ever did, weighing about 141 pounds on admission. Of course that is due to the fact that the accumulating ascites and simultaneous loss of fat and muscle substance have apparently gone parallel, so that now she weighs her best normal weight with what she has noted—loss of flesh—and the loss of flesh made up by a gain in the ascitic fluid which we have noted.

As to her present illness—six months ago the patient was perfectly well as far as any symptoms were concerned. She has had no pain, no subjective signs or discomfort except itching of the skin and increased discomfort from an enlarged abdomen and swelling of the legs, to be described later. These symptoms began six months ago, and prior to that she had no symptoms, and those are the only symptoms she has had—itching of the skin, enlargement of the abdomen, and swelling of the legs. At present she feels well, and only yesterday stood on the street all day long viewing the parade (that was the peace celebration parade). The first trouble the patient noticed was itching and irritation of the skin which was probably most severe five to six

months ago. So intense was the itching that she excoriated herself from scratching the lesions. On the skin of the abdomen there was a sensation as though small insects were burrowing into the flesh. Besides on her abdomen the irritation was intense on the arms and legs. She thinks she was somewhat jaundiced at this time. She consulted a doctor, who told her that she had liver trouble, but gave her little advice as to the nature of the condition. The itching on the skin has diminished gradually and has given very little discomfort in the past month. At present there is very slight irritation. About six months ago the patient, though feeling well, noticed that she could sleep for three to four hours in the afternoon, so that she regularly did this. She was able to keep awake if she had any work that she was obliged to do. Her skin was of a rather yellowish hue, but this was not pronounced.

One month ago, while taking care of a patient sick with influenza, where she worked very hard, she suddenly became aware of a considerable swelling of the ankles and legs and her knees were particularly swollen. The swelling was hard and did not yield to pressure. At this time she consulted a physician, who told her that he was unable to account for it. The abdomen was swollen at this time and she says that during the following week she noticed it becoming rapidly distended. She doubts if it was a gradual increase in size which she had failed to notice, but regards her distention as having come on rapidly in the course of a week's time. According to her statement her jaundice increased in the past month, but she did not notice the scleræ to be yellow until entrance to the hospital, when her attention was called to it. On one occasion one month ago she noticed her urine to be very dark. She has always observed her urine, and says that it has been dark at intervals since then. About the same time her stool was of a light yellow color and she noticed a similar condition only once since, and that was the morning of admission. The patient says that she has never had any pain at any time and that she feels strong and healthy. She believes her flesh has fallen away considerably in the last few months, and she thinks that the only reason her weight is

maintained is because of the swelling of her abdomen. Having been thrown with patients as an attendant, though not a graduate nurse, that history probably represents a more intelligent observation of herself than we generally get in our patients, and it is a pretty clear history.

The physical examination is essentially negative except for the points that have been brought out, that is, pigmentation and fluid in her abdomen—she has been tapped on three occasions. On November 13th 3900 c.c. of yellow turbid fluid was removed, having a specific gravity of 1005, 5.8 grams of albumin per liter, quantitated with the Esbach method, which is only moderately accurate, no bile, no urobilin, 280 cells per centimeter; lymphocytes, 45 per cent.; mesothelial cells, 55 per cent. She was tapped again two days later and 1800 c.c. of the same kind of fluid was removed, specific gravity 1008, cell count 2670, 89 per cent. polymorphonuclears, 11 per cent. lymphocytes. The albumin in this specimen was slightly less, 4.8 grams per liter. On December 2d 3500 c.c. were removed, giving a specific gravity of 1006, 8 grams of albumin per liter, and 200 cells, 50 per cent. of which were lymphocytes, 47 per cent. mononuclears, in other words, mesothelial cells, and 3 per cent. polymorphonuclears. In the counting chamber it was observed that some of the cells contained rather numerous brown pigment granules.

She has not any leukocytosis. There is a slight degree of anemia; 4,008,000 red cells, with a hemoglobin of 85 per cent. The differential count is normal and there is nothing abnormal about the red cells. Her urine specific gravity has averaged from 1010 to 1030 at different observations. Occasionally it contains the slightest possible trace of albumin, but is usually free from albumin. It usually contains a very small amount of glucose. From time to time it has given a positive bile test. There are no red cells in the urine in most of the examinations, sometimes an occasional one. A few white cells are ordinarily found, but no casts have been found in a number of observations. One stool examined on November 14th was small, dark, fluid, no gross blood, pus, or mucus. Benzidin reaction was negative. Nothing abnormal was found microscopically in the

stool. On November 25th a stool was examined, which was clay colored, soft, unformed, no gross blood, pus or mucus, negative benzidin reaction. On the 26th the stool was clay colored, soft, unformed, no gross blood, pus or mucus, benzidin negative. There was a certain amount of diarrhea—four stools that day. Since then a number of stools have shown a negative benzidin test. Fairly abundant fatty acid crystals were noted in a number of the stools. The Wassermann reaction was negative. The blood-pressure is 140 systolic and 90 diastolic.

Mr. ——, what should you say about the diagnosis? What would you consider as the probable condition with that history and that physical examination?

STUDENT: Jaundice of one type or another.

DR. CHRISTIAN: Yes, the patient has jaundice. Of what type do you think it is?

STUDENT: The chronic type or probably a sort of catarrhal jaundice.

DR. CHRISTIAN: Do not say "catarrhal" unless you know what it means, and that you really mean it at this time. What do you mean by "catarrhal jaundice"?

STUDENT: Jaundice due to catarrhal inflammation of the bile-ducts, and possibly extending into the liver along the smaller ducts.

DR. CHRISTIAN: Catarrhal jaundice is a pretty definite clinical entity—jaundice without any evidence of any gross lesion in the liver, coming on acutely, usually associated with or preceded by a gastro-intestinal upset, moderate in nature, accompanied by fever in the early stages and the fever and gastro-intestinal upset clearing up, but the jaundice persisting over relatively a short time, a few days to a few weeks. Here is a patient that has had jaundice for a considerable length of time, so it is not catarrhal jaundice, and you do not want to use that term. What evidence have you as to a cause of the jaundice? What evidence have you in the patient of any other abnormality besides jaundice?

STUDENT: There is the cardiac lesion.

DR. CHRISTIAN: Which you said she did not have. Why do you say she has a cardiac lesion?

STUDENT: She has a systolic murmur, heard at the base.

DR. CHRISTIAN: What is the presumptive evidence about systolic murmurs at the base?

STUDENT: That they are functional.

DR. CHRISTIAN: Yes; so there is not much to stand on as evidence of a heart lesion. She might have a heart lesion, but with those findings as regards the murmur the burden of proof is on the lesion side. The presumptive evidence is that any patient with a basal systolic murmur has a normal heart until you prove that it is diseased in some way, decreased in function or increased in size. What does the accumulation of fluid in the abdomen suggest?

STUDENT: A sclerotic liver, syphilitic or alcoholic.

DR. CHRISTIAN: What term do we generally use when the liver is sclerosed?

STUDENT: Cirrhosis.

DR. CHRISTIAN: Yellow—it is an old term that goes back a great many years. It was used for the color of the liver, but, as the cirrhotic liver is not always yellow, when we use the term "cirrhotic," we mean now a liver with increased connective tissues in it and not the original meaning of the term. Why do you say that she probably has cirrhosis?

STUDENT: It is suggested by the ascites and interference with the portal circulation. The edema of the legs would not be so suggestive of it.

DR. CHRISTIAN: How would you explain the edema of the legs here?

STUDENT: Possibly the fluid in the abdomen would interfere with the return from the legs by pressure on the femoral veins.

DR. CHRISTIAN: Are the femoral veins in the abdomen?

STUDENT: As they pass up they are.

DR. CHRISTIAN: After they pass up, what are they?

STUDENT: The inferior vena cava.

DR. CHRISTIAN: I mean as they pass up to enter the inferior vena cava. There is the inferior vena cava (illustration on the board) and here are the femorals, what is in between?

STUDENT: You have the femorals and then the iliacs. There

are two sets, the common dividing into the external iliac and the internal iliac.

DR. CHRISTIAN: You have the inferior vena cava, the common iliac and the external and internal iliacs, and pressure on those in the abdomen will cause edema of the legs. What is it that causes stoppage of the circulation to the legs—what is the mechanism?

STUDENT: Distention of the abdomen probably is sufficient; that is, stretching of the abdominal wall is sufficient, though the pressure probably does not reach that point.

DR. CHRISTIAN: What point would it have to reach?

STUDENT: Complete closure of the veins, which would necessitate the overcoming of the various factors that produce venous circulation.

DR. CHRISTIAN: What is the pressure in the inferior vena cava?

STUDENT: Negative pressure.

DR. CHRISTIAN: What keeps the circulation from stopping if the pressure in the vein is low? Of course in the lower part of the inferior vena cava and iliacs the pressure is not a negative pressure, but is a low pressure and is a slightly positive pressure. That being so, why are not those veins blotted out and the circulation stopped?

STUDENT: The action of the valves and the pumping action of the diaphragm prevents it, and there is slight pressure from the arterial circulation.

DR. CHRISTIAN: Yes, slight pressure from all of those things come in. First, there is not any interference with the onward flow of the arterial supply. The arteries carry blood to the legs which must come back and can go against very considerable resistance as long as there is a good driving impulse in the heart forcing the arterial circulation. Why are the arteries more resistant than the veins?

STUDENT: They are deeper in.

DR. CHRISTIAN: What other difference?

STUDENT: They are thicker walled and have higher internal pressure.

DR. CHRISTIAN: They are much thicker walled and so rather better protected. If the arteries and veins were built alike and had the same pressure these circulatory disturbances from accumulating abdominal fluid would be a much more serious matter. As a rule you get what this patient has, simply a moderate degree of edema of the legs except that sometimes, with interference to the circulation and slowed venous circulation, there is a tendency to thrombus formation, and you get thrombi forming either in the veins in the abdomen or down the leg, and you get added to that picture venous thrombosis. These patients not infrequently have thrombosed veins in addition to having edema. The edema of the legs is most probably due to the ascites. How could you prove whether it was due to the ascites or not?

STUDENT: It ought to be reduced, if due to the ascites, when the abdomen was tapped.

DR. CHRISTIAN: If you mechanically can remove the fluid and keep it from recurring, in a short time the edema of the legs will disappear. Practically it is frequently rather difficult to carry out that test because the abdomen fills so promptly after it is tapped that it fills up again before the edema has time to drain away from the legs, but when there is a question of edema of the legs being due to ascites we observe to see whether tapping of the abdomen relieves the edema.

Did that happen in this case, Dr. ——?

DR. ——: Yes, it did.

DR. CHRISTIAN: It has been relieved after tapping, and the edema gets more marked when the abdomen becomes more distended. We have evidence of a certain degree of jaundice which suggests interference with the biliary function and points to some hepatic lesion. We have the ascites, which suggests that there is interference with the portal drainage, and that suggests either a lesion in the liver or a lesion in the portal vein that is obstructive in nature like thrombosis of the portal vein or disturbance in the circulation through the liver, such as is produced by cirrhosis, so the jaundice and ascites point to cirrhosis of the liver. The liver is a little enlarged, which is in

accord with the idea of cirrhosis, but does not prove cirrhosis. The spleen is moderately enlarged. What explanation could you give of that? In other words, what causes enlargement of the spleen?

STUDENT: In this case it seems as if with the liver cirrhotic the back-pressure might cause a certain amount of congestion of the spleen and enlargement.

DR. CHRISTIAN: Yes, the liver may be cirrhotic and the spleen simply enlarge on account of the congestion—passive congestion—brought about from interference in the portal circulation. What other changes cause enlargement of the spleen besides back-pressure from a cirrhotic liver?

STUDENT: Various conditions of hyperplasia from chronic or acute infections.

DR. CHRISTIAN: Yes, various chronic hyperplasias. Marked increase in the size of the spleen is the result of chronic hyperplasia and that effects both the connective tissues in the spleen and the amount of cellular elements in the spleen. Very often with cirrhosis of the liver the spleen is enlarged beyond what you would expect from portal obstruction, and we say that, because the same kind of obstruction, brought about from poor circulation on account of a heart condition, having just the same effect as far as back-pressure on the portal system is concerned, as a rule, does not produce any marked enlargement of the spleen, but produces a moderately enlarged spleen, whereas cirrhosis of the liver patients may have a markedly enlarged spleen. You have already seen a case of this type with enlarged spleen. Dr. Wolbach showed you one that belonged in the group of Banti's disease in which there was some other cause for the enlargement of the spleen than enlargement simply from back-pressure. In this patient the splenic enlargement may be only the result of cirrhosis of the liver or may be from some chronic inflammatory change leading to hyperplasia. Is there anything in this history to suggest in this particular case that the change in the spleen is one or the other?

STUDENT: The blood is essentially negative, which would tend to exclude infections, as there is no leukocytosis.

DR. CHRISTIAN: Chronic infections probably would not give a leukocytosis, and chronic splenic hyperplasia usually has a normal blood-picture. What is there in the patient's history? How long has the abdomen been enlarged? Her abdomen swelled three weeks ago and her legs were noticed to be swollen four weeks ago. She thinks these changes came on pretty definitely at that time. Assuming that the edema of the legs is due to change in her abdomen, and the abdomen showed some swelling when the legs were noticed to be swollen, that would take it back a month, or, to make it prior to that a reasonable length of time, we say the abdomen has been enlarged for six weeks; that is hardly long enough, from the point of view of passive congestion, to cause a moderately enlarged firm spleen, so if her spleen is definitely enlarged and firm, as suggested by some of the observations, presumably there has been some hyperplastic process going on in the spleen and it is not simply a question of back-pressure.

What about the color of the skin apart from jaundice? You have evidence of jaundice with a little yellow color to her scleræ. We have found bile present in her urine, and that is further borne out by the fact that there is a decreased amount of bile in her stool. Some of the stools are clay colored without being essentially fatty stools. Bile, however, is not absent from the stool. When tested for it is found. At times it is present in enough quantity to color the specimen. How about the pigment in the skin?

STUDENT: It is darker than the ordinary pigment of jaundice. It suggests more Addison's disease. It is brownish almost.

DR. CHRISTIAN: It is a dark pigment, not particularly a yellow pigment, such as we see in jaundiced cases, nor has it the greenish hue that we often get in long-standing cases of jaundice. It is pigment which is of a distinctly brownish color and mixed with it there is probably a certain amount of jaundice, but, as you look at the hands, abdomen, and face your impression is not one of a jaundiced patient, but of an individual who is pigmented, and the pigment is, in general, of a brownish color. Her history is one of pigmentation certainly

going back about six months. She then noticed that she was yellow, and associated with that was the marked itching that we get in jaundice and which leads to a great deal of scratching. Then she says that she has always been very dark in color. She is, of course, a dark brunette, and there is a certain amount of doubt in her mind as to whether she is much more darkly pigmented now than she was in the past. She speaks of being periodically darker in color and always being pretty dark, so she is not quite sure of how long this dark pigmentation has been going on. It may date back to her early girlhood or it may be a thing that increased fairly recently, but increased gradually enough so that she herself really has not noticed any marked amount of pigmentation in the sense of change. If you did not know about that point, looking at her you would say that she was very definitely pigmented. We do not see Irish brunettes as darkly pigmented as her skin is and, as you say, that is somewhat suggestive of Addison's disease. She has a pigmented skin interrupted by non-pigmented spots, which are areas of vitiligo. Vitiligo occurs in non-pigmented people, but is particularly prominent when it occurs in pigmented people. The negro, particularly the mulatto type, very often shows vitiligo. Of course the negro has the same kind of pigment as a case of Addison's disease, except he has rather more of it, and has always had it, and the next generation is going to have it. Addison's disease is an acquired pigment, but as far as the skin is concerned there is no difference between Addison's disease in a microscopic section and the pigment in the negro.

December 12, 1918.

I want to discuss first this afternoon the diagnosis of the patient that I showed on Monday. To sum up what we found in that case, we had a woman of forty-four, who presented the picture of marked ascites with moderate edema of the legs. Her skin was deeply pigmented, brownish in color, with spots of vitiligo. In addition, there was a very slight degree of jaundice. Her abdomen had been tapped several times. After the removal of the fluid the liver and spleen could be felt and were

found to be moderately enlarged. She had a normal heart, normal lungs, and no signs of nephritis. For eight years she had had nosebleeds accompanying her menstrual periods occasionally. For two years this phenomenon had been absent with the exception of one menstrual period when she had a nosebleed, and that was her last menstrual period and, apparently, the beginning of her menopause. She was unusually well up to six months ago. Then she began to have severe itching of the skin, so much so that she scratched enough to cause excoriation of the skin. At that time she noticed that she was jaundiced. A month ago she noticed swelling of her legs, and at this time she noted swelling of her abdomen. It is not very clear from her statement whether the swelling in the abdomen antedated the swelling of the legs or not; apparently she noticed the swelling of the legs first and then noticed the enlargement of her abdomen. She feels pretty certain that swelling of the abdomen took place in a relatively short time and was not present until approximately a month ago. As to her skin color—she thinks that she has always been dark, and apparently she had not noticed particularly this dark brown color to her skin as being anything abnormal, though she had noticed six months ago that she was jaundiced. There has been a loss of weight compensated by increasing fluid, so that she has noted increasing emaciation, and yet on admission her weight was the same as it was at her best weight when she was well. There was no history of use of alcohol and no venereal disease by history, symptoms or signs, and her blood Wassermann reaction was negative.

That case raises the question of the nature of the hepatic lesion, because the evidence is pretty clear that there is a disturbance in the liver, and the question of the nature of the pigmentation. It seems pretty clear that the change in the liver is of the nature of a cirrhosis, possibly associated with obstruction in her common bile-duct, that the ascites is secondary to the portal obstruction, that the swelling of the legs is due to the accumulation of fluid in the abdomen pressing upon the inferior vena cava or some of its intra-abdominal branches. The enlargement of the spleen may be the result of the portal

obstruction or may be due to some process of hyperplastic nature going along with the change in the liver. That the latter is the case is suggested by the fact that the spleen is of considerable size, when apparently from her symptoms the portal obstruction has been of short duration. As far as the pigment in the skin is concerned vitiligo is probably an accidental accompaniment and has no significance. Six months ago she had itching and noticed jaundice. Apparently the intensity of the jaundice was not very great. The itching, however, accompanying the jaundice was sufficient to cause vigorous scratching and suggests that at that time there undoubtedly was a disturbance of the nature of jaundice because itching is a very common accompaniment of jaundice, though it does not run parallel in amount to the jaundice. Some of the patients with the most marked itching have very little jaundice, and some of the patients with very marked jaundice have very little or no itching of the skin. In other words, pruritis is a common accompaniment of jaundice, but does not occur directly in proportion to either the extent or the duration of the jaundice. She was probably pigmented, from her story, in addition to the jaundice at the time of the development of the jaundice and the itching. In other words, she had a brownish pigmentation at that time and possibly has had it for a long time. At the same time she is abnormally deeply pigmented for a woman of her race, she being an Irish woman. Although she is a brunette, you would not expect her skin to be as dark as it is unless there were some pathologic condition.

What conditions cause a combination of cirrhosis with enlargement of the spleen and pigmentation of the skin? The condition that you have to think of with her associated symptoms is hemochromatosis. Hemochromatosis is a condition in which there is an abnormal deposition of iron-containing pigment in the connective-tissue cells of various parts of the body, in the skin causing discoloration, in the liver causing, or at least associated with, connective-tissue increase and the pathologic picture of a chronic interstitial hepatitis, in the spleen associated with hyperplasia, possibly causing hyperplasia, in the pancreas

causing interstitial pancreatitis with connective tissue increase, and in the pancreas usually deposited also in the cells of the islands of Langerhans, and associated with these changes disturbance of carbohydrate metabolism leading in the large majority of cases to actual diabetes, the so-called bronzed diabetes.

This particular patient of ours in all urine examinations has shown a very slight amount of glucose in the urine; in other words, a slight degree of glycosuria, present in small amount when the patient is not on a carbohydrate-limited diet.

The pigment of hemochromatosis is also deposited in other organs of the body, though in other organs of the body it rarely ever causes enough change to lead to symptoms. The pigmentation is increased in amount in the heart muscle and yet the heart usually functions normally. It is increased in the kidney, though there is usually no connective tissue increase in the kidney and nothing to suggest chronic interstitial nephritis as a result of the deposition of the pigment. It is increased in the striated muscle of the body in general and increased in the smooth muscle. Very often there is a considerable deposition in the smooth muscle of the corium.

So much for the general picture of hemochromatosis. There is a good deal in what I have said in summing up this case that is in agreement with hemochromatosis. Against hemochromatosis in this particular case is the history of jaundice occurring six months ago, apparently persisting for some time, as indicated by the itching, and present prior to the development of the ascites. Her ascites is against hemochromatosis because most of the cases of hemochromatosis whereas they have a cirrhotic change in the liver do not have portal obstruction and ascites. The sex of the patient is in a sense against hemochromatosis because of a very considerable number of cases reported in literature nearly all have occurred in males. I believe, in a group of cases which Futcher reported of 36 patients, 2 were females and 34 males. Of course this may be the unusual case, and the relative infrequency in females of the disease is no justification for excluding that diagnosis in this individual case.

Does the glycosuria necessarily indicate a lesion in the pan-

creas presumably due to the deposition of the pigment, and is that part of the picture of hemochromatosis? Usually cases of hemochromatosis when they develop glycosuria have glycosuria of the extent and character of the average diabetic, glycosuria considerable in amount when the patient is on a diet with an average amount of carbohydrate, and frequently a glycosuria which persists even with a great reduction of carbohydrate intake just as you get in diabetes. However, typical hemochromatosis with typical lesions in the pancreas may show only a slight glycosuria, may show a transient glycosuria, or may show no glycosuria at all. We have observed cases in this hospital which were proved at autopsy to be typical cases of hemochromatosis in which glycosuria was a very trifling and transient symptom over a very considerable observation in the hospital with the patient on a free carbohydrate diet.

The ascitic fluid of a case of cirrhosis very frequently contains a small amount of glucose, so that you get a positive Fehling test. I believe in this particular case there was no glucose in the ascitic fluid, but the finding of glucose in ascitic fluid is not at all a surprising accompaniment of ascites from cirrhosis of the liver. A slight degree of glycosuria is very common in chronic conditions where there is no evidence of diabetes. Such a condition is represented by hypertension with slight renal lesion. A good number of our cases of hypertension show slight degrees of glycosuria. Slight degrees of glycosuria are not uncommon in simple cases of chronic cirrhosis without any pigmentation, so that one factor, though suggesting hemochromatosis, is not definite.

The pigmentation in itself in this particular case is rather more of a brownish color than you usually get in hemochromatosis. Hemochromatosis is much more apt to have a reddish hue. Here is a Lumière plate (Fig. 235) of one of our earlier cases (Med. No. 3957), a man who remained in the hospital for the better part of two and one-half years, and you will see there distinctly the reddish or copper-red color. This man, like the present patient, was of Irish extraction, had the Irish sense of humor, and rather liked to boast of the fact that he was the only living

Irish Indian. He did have that sort of copper-reddish brown color that is characteristic of the Indian. This pigment then in itself as far as color goes is not characteristic of hemochromatosis, though I have seen cases of hemochromatosis in which the discoloration was quite similar to this particular case.

What is the cause of hemochromatosis? Is there anything in the nature of the lesion that will give us help in making a diagnosis? The type of pigmentation is, as I have already described, a diffuse one. If you are interested in the pathology there is a very good pathologic discussion of hemochromatosis in the Archives of Internal Medicine, 1911, vii, 75, by Sprunt, with photographs showing the distribution in the tissues of the pigment and a discussion of the pathogenesis of the disease. After reading the various discussions of the disease, as outlined by Sprunt, you can sum it up as to etiology by saying that Dr. Sprunt and the rest of us do not know very much about it. That article was written in 1911. Since then there has been experimental work that throws some light on the possible mechanism of the production of the condition. In a paper published in November of this year in the Journal of Experimental Medicine (1918, xxviii, 629) Dr. Rous and Dr. Oliver reported the production in animals of what they called experimental hemochromatosis. It was produced in rabbits in which animal plethora had been produced by repeated injections of blood. These injections of blood were carried out in connection with some other experiments in which they were studying the fate of red blood-corpuscles when injected into animals. They noticed that their experimental animals showed pigmentation, and the pigmentation in character and distribution was quite similar to the pigmentation of hemochromatosis. Then they found, like other observers, that there was a certain amount of pigment deposited in the kidney, and they observed in the urine the appearances of cells containing pigment, and that suggested in their minds that this might be a possible diagnostic help in hemochromatosis. Subsequently they had the opportunity to study the urine of a case of hemochromatosis in the hospital, and they found there pigmented cells in the urine, and as a re-

FIG. 235.—A case of true hemochromatosis referred to in comparison with the patient discussed in the clinic.

sult of that Dr. Rous in the same journal published another paper entitled "Urinary Siderosis," with pictures of the kidney and the pigmented cells in the urine (Jour. Exp. Med., 1918, xxviii, 645). That case subsequently died, and at autopsy it was seen to be a case of hemochromatosis. That work suggests that the cause of the disease is some destructive process in the red cells leading to breaking up of the red cells at an unusual rate with deposition of the pigment, set free in that breaking up, in various connective-tissue cells of the body, with possibly a certain amount of metabolic change in the pigment, leading to the deposition of hematoidin, a by-product of hemoglobin, not possessing the pigmentary characteristics of hemoglobin, but a pigment containing iron, which will give the test for iron when the proper stains are used. If Rous' idea is true then cases of hemochromatosis should be anemic unless blood regeneration is active enough to keep pace with blood destruction. If blood regeneration is active enough to keep pace with blood destruction and prevent anemia, then at autopsy these cases should show signs of hyperplasia in the structures that form red blood-cells, namely, in the bone-marrow. Our patient showed, as I said, very little anemia. I gave you her hemoglobin, which is very little below normal, and this is true of most cases, and anemia is not a common accompaniment of hemochromatosis, and our case agrees in that particular with typical cases of hemochromatosis. These cases do not suggest having had a plethora of blood. Also it is true that the bone-marrow in this case is not likely to be a hyperplastic bone-marrow; as there is no evidence of active blood regeneration this explanation of Rous may not fit in with the actual conditions in the human cases, though it is suggestive.

Another view, which was advanced first, I think, by Meltzer some years ago, without very much proof for it, was that the pigmentation is not due to destruction of red cells, is not associated with any form of potential or real anemia, but is due to disturbance in the metabolism, which leads to a storing of iron in the body because the ingested iron which is present in much of the food instead of being excreted is converted into some

form not easily excreted, and after absorption is deposited in the tissues. Recently there have been some studies to see whether in the human being with hemochromatosis there is a disturbance in the iron metabolism. Dr. Stevens, who was for a short time Assistant Resident in this hospital, with Dr. Campbell Howard of Iowa City, studied the metabolism in a human case, and they published their results in the Archives of Internal Medicine, 1917, xx, 896, and they gave what the literature had on the question of iron metabolism prior to that time. They studied a case rather late in the course of the disease. They found evidence of a slight storing of food iron without any signs of undue destruction of blood-cells. Their method was to put the patient on a fixed diet, which the patient could take daily for a period of six to seven days. They studied the urine and studied the feces during that time, quantitating the iron in the intake of food and quantitating the iron in the output of feces and urine. The striking thing about their observations is that the urine chemically showed no iron. The iron that was excreted was excreted by the gastro-intestinal tract, was found in the stools, but was not found in the urine. You will still find on page 899 of that article a table of intake of iron in milligrams and the output in the urine. The patient was studied for five weeks in this way. Their findings you see are not exactly in accord with the observations of Rous, who found iron in the urine, unless it is explained by the fact that the iron in the urine is in the cells and that the cells were sedimented out, and they chemically quantitated the iron in the urine after the sedimentation had taken place. That is not at all improbable, because these are rather slow and tedious chemical methods, and I have no doubt that the urine stood for some time in the ice-box while other work was going on, and the sediment may have gone to the bottom and not been quantitated.

Dr. McClure published in the Archives of Internal Medicine for November, (1918, xxii, 610) a similar metabolic study carried out here in this hospital in one of our cases of hemochromatosis, with essentially the same result, the finding of a stored amount of iron, the food intake of iron being greater than the

iron recovered in the stools, none being found in the urine. If you look up those figures you will find that the amounts of iron are pretty small, and it is not at all improbable that the discrepancy between the intake and the output, which is a small one, may be due to errors in technic and methods of observations, but both studies agree in finding a stored amount of iron, and they are suggestive of that mechanism of the production of the lesion, putting the disease in the group of metabolic disturbances and a disturbance in the metabolism of iron. Unfortunately, there have not been any very extensive studies, under normal conditions or in other diseases, of iron metabolism, and there is not any very satisfactory data with which to compare these studies. Until that is done I do not think that we can feel too sure that there is an actual disturbance of the iron metabolism.

This particular patient has not had an iron metabolism study. We have excised a piece of skin, and that skin shows a fairly definite increase in the pigment in the lower layer of the epithelium. You remember that in the lower layers of the epithelium of the skin there are cuboidal cells, and then the cells become more and more flattened out in the upper layers until you get to the horny layer. Normally in those lower cells there is a deposition of a varying amount of pigment, always present in the skin, more abundant in dark-colored people than in people with a light-colored skin. In this case there is more than the normal amount of pigment in that layer and in some of the upper cells, and that pigment under the microscope is seen to be made up of rather coarse granules of brownish or, better, yellowish color. In the subcutis are single connective-tissue cells with coarse granules of pigment of the same type pretty thickly studding the cell. There is not any particular amount of pigment around the sebaceous glands or sweat-glands, and no increased pigment in the smooth muscle of the deeper layers of the skin. These connective-tissue cells are to be regarded as chromatophores, probably cells normally pigmented. Whether that pigment is iron containing or not I will have to report later, because the first piece of skin excised was

hardened in Zenker's fluid, and stains to demonstrate iron do not work very satisfactorily after Zenker fixation. There is a bit hardened in alcohol going through now, but the Pathological Department has not completed the staining.

We have examined the urine of this patient to see if any pigmented cells were present in the urine that gave the iron reaction, and we found that there was a certain amount of iron-containing pigment, but we were skeptical, as we should be, and I suggested to Dr. Balyeat, who made the test, that it was very important to take the urine from somebody else supposedly normal and carry out the same procedure, and he found about the same amount of apparently iron-containing pigment in the normal individual. What its source is I do not know. Some of the cells from the urine of this patient and I think from the ascitic fluid have been run through and stained for iron, and there are pigmented cells in both places which seem to show the iron reaction.

Now we have the evidence of pigment in the skin, have some evidence of iron-containing pigment in the ascitic fluid and in the urine from this case, but I am still quite skeptical as to whether that represents a diagnostic point that justifies us in saying that this is a case of hemochromatosis or not. You have to attach a good deal of importance, I think, in this particular case to the fact that this woman is intelligent, that she has given an exceedingly good story of the onset of her symptoms, and apparently her observations have been accurate. She herself has not noticed any rapid change in her skin, she thinks that she has been pigmented for a long time, probably ever since she was a young girl. Then we have that history of jaundice and itching, which would agree with the diagnosis of some biliary disturbance causing jaundice, and, with the itching of the skin, of having to scratch a good deal. That irritation may have led to pigmentation, but I feel skeptical from her history of scratching, etc., that it was sufficient to cause an increase in pigmentation, though, if already there was a pretty marked pigmentation, it might be accentuated as a result of scratching. It is well-known that irritation of various kinds

from the pruritus of jaundice to the itching from lice leads to scratching, and that scratching leads to pigmentation. The vagabond is often a pigmented fellow after you get the dirt off and can see the skin. Then there is a variety of pathologic conditions causing increased pigment varying all the way from chronic ascites to solid ovarian tumors, tubercular peritonitis, etc. Another of the causes of pigmentation is a chronic renal condition. These cases of chronic jaundice with itching sometimes become very much pigmented, and you have a great deal of difficulty in a number of cases in determining whether the pigment is abnormal in the sense of hemochromatosis or whether the pigment represents an extension of the normal pigment of the skin due to various irritating causes, or whether the pigment is really of biliary origin.

On the whole, I am a little inclined to think that this patient represents a case of simple cirrhosis of the liver with ascites in a woman pretty dark to start with, and her pigment accentuated by scratching and with possibly an added factor in a chronic irritation in the peritoneal cavity in the nature of ascites, such as we find in solid ovarian tumors, etc. An association of the pigmentation with changes in the adrenal has not been excluded, but the case is not similar to the usual case of Addison's disease.

Hemochromatosis is rather a rare condition. For instance, up to 1912 Potter and Milne could find only 50 cases of bronzed diabetes, that is, hemochromatosis with diabetes. Since then, of course, a good many cases have been added to the literature. That paper in the American Journal of Medical Sciences (1912, cxlii, 46), by Potter and Milne, gives all the reported cases up to that time and discusses them, and is a useful summary of the literature.

January 20, 1919.

One of the men asked in regard to the findings in the skin in that patient (Med. No. 9841) that I showed you some time before Christmas with marked enlargement of the liver, etc., where there was a question of hemochromatosis. The skin shows an increased amount of pigmentation, and that pigmentation so far as the pathologists have been able to determine is not

an iron-containing pigment or a pigment that gives the iron reaction. There is a considerable amount of pigment in the lowest layer of the epithelium, and that looks just like the normal pigment of pigmented skin such as you get in the negro, or the kind of pigment that you get following an irritation, such as sunburn. Then the connective-tissue cells in the skin have more than the normal amount of pigment, and that pigment is fairly coarsely granular, brownish-yellow in color under the microscope, and is deposited in practically all of the connective-tissue cells. Apparently no pigment was found in the smooth muscle. I compared that pigment this morning with sections from a previous case known to be hemochromatosis, and the pigment is in slightly smaller granules, but otherwise looks pretty much the same; but so far as that study goes there is no positive, definite evidence that that is the kind of pigment we get in hemochromatosis. On the other hand, it may be an iron-containing pigment in which technically we failed to demonstrate iron, or it may be a case of hemochromatosis and the skin pigment not contain iron. Such cases are reported.

The patient has remained in the hospital, and my impression is that in an interval of about three weeks when I was away from Boston and did not see her that the pigmentation has increased. It looks like a darker pigmentation. That is merely an impression; we have used no accurate way of measuring such changes. There has been no other change in her condition except pain in her abdomen. This has increased and radiates now down her legs. She continues to show a trace of sugar in her urine. The findings are perfectly consistent with hemochromatosis, but we have no positive proof that it is hemochromatosis, and I am inclined to think it is not hemochromatosis.

February 19, 1919.

I want to report on a case which has not changed much since you saw her—the woman (Med. No. 9841) with the marked pigmentation, moderate enlargement of the liver and spleen, in which we raised the question of her having hemochromatosis, but in the skin of whom could not be demonstrated any iron in

the pigment. The patient has not changed very much in general appearance, but there is a question as to whether the pigment has not moderately deepened. From time to time she fills up with fluid and requires that her abdomen be tapped. Following the tapping she now has a considerable amount of pain, and all the time she has a sort of constant pain in her abdomen which tends to radiate down her legs, and is severe enough so that she has to have some opiate to make her comfortable. I do not think that at the time we had her in the clinic that she was complaining very much from pain or suffering any great amount of discomfort, except simply discomfort from the distention of the abdomen, so that feature has been added, and the nature of the pain radiating down the legs suggests some form of pressure on nerves, and in that way the pain referred down the legs. After she is tapped the abdomen feels just as it did before; you can feel the liver edge beneath the costal margin and you can feel the spleen two or three finger-breadths down on the other side. There is now pretty definite spasticity of the lateral abdominal muscles, but no spasm and no definite mass of any kind can be felt in the abdomen beyond the liver and the spleen. You remember that that patient gave also the history of jaundice. She shows a slight degree of jaundice now and she has bile in her urine. Her stools are clay colored. There is nothing definite to be added in the way of a diagnosis further than to say that as it progresses it has not become any more clearly a case of hemochromatosis, and the pain is somewhat suggestive that there may be something like a neoplasm in the retroperitoneal tissues, but there is nothing positive of that. There is evidence of portal obstruction causing ascites and evidence of an intrahepatic disturbance causing the jaundice and of obstruction to the flow of bile into the intestine. As far as that goes, it fits in with the idea that it is a case of cirrhosis, possibly with a stone in the common duct. Of course, it would be cirrhosis if it were a case of hemochromatosis. The iron pigment in hemochromatosis is deposited in the increased connective tissue in the liver. There has been no change as regards the glycosuria. It is still present in small

amount, but there is not a definite diabetes. I will report later on that patient as to any changes. She is still on the ward.

March 17, 1919.

This (P. B. B. H., Med. No. 9841) is the patient that I showed in the clinic of December 9th and 12th, and reported about on January 20th, and again on February 19th. She has been in the hospital a total of one hundred and twenty-four days. Her abdomen has been tapped twelve times, and from 6 to 7 liters of fluid removed each time. There has been no change as regards the glycosuria. Her general condition has remained as described at the last report. She has had this persistent discomfort which requires an opiate. Sometimes following the tapping she has had a very considerable degree of pain in her abdomen which decreases after she begins to fill up again, but it never disappears. Following one tapping one of the house-officers thought that he could make out a mass, which was irregular and firm, in the retroperitoneal region of the epigastrium. Following previous and subsequent tappings nothing definite of this nature had been made out, and it seems rather probable that what was made out was the liver and not some other mass. She has continued to have bile in her urine, and you can see, I am sure, that now she is pretty deeply jaundiced. Her conjunctivæ are definitely yellow. In places in the brownish color she has, as she had when you saw her several months ago, areas of vitiligo. The abdomen shows more of the brown color than her face and extremities, as it did before, and with this there is intermixed a certain amount of yellowish tinting, and these patches of vitiligo show some slight yellowish color; in other words, where the brown is not so dark there is quite evident jaundice. She has persistently had clay-colored stools, and associated with that there has recently been some diarrhea. The stools have not now for a long time shown any color indicating bile, and such bile tests as have been made have been negative. You probably recall that early in her stay in the hospital the stools were not clay colored, and a little later, though the stools were very pale, bile was demonstrated in them. As she has progressed in her illness jaundice has become much

more an evident feature in the case. There was a history of jaundice in the beginning, and very slight jaundice was present when she came into the hospital. That jaundice has become more marked and the element of obstruction has become more marked; that is, there has been no bile in her stools while her jaundice has been increasing, so that, as it stands today, just what I said in regard to the diagnosis before, I think, holds good. There is evidence of an intrahepatic disturbance causing the enlargement of the liver; in other words, a form of hepatitis; the spleen is enlarged, splenitis, and associated with that there is jaundice and also evidence of biliary obstruction. Though you cannot say just what the biliary obstruction is due to, the whole history is rather more suggestive that the biliary obstruction is due to gall-stones than that it is due to neoplasm obstructing the common duct. There is not any history of pain, there is no recurring fever, as you often get with stone in the common duct, and, as I have repeatedly said, there is no definite evidence to exclude a neoplasm. In the beginning the condition seemed to be one that fitted in better with an intrahepatic disturbance than a neoplasm; to this has been added definite evidence of biliary obstruction. There are no other features that have developed in the case besides the ones that I have mentioned.

March 31, 1919.

The patient (P. B. B. H. Med., No. 9841), recently shown, rapidly lost ground and died. Autopsy today showed a very marked cirrhosis of the liver with an associated chronic splenitis. The liver was a rich green in color with a nodular surface; it weighed 940 grams. The spleen weighed 400 grams. There were no stones in the biliary tract; the ducts were patent and showed no evidences of having been obstructed. The pancreas, though firm, seemed normal. The intense jaundice had resulted from intrahepatic changes and these must have caused the acholuric appearance of the stools. Judging from the fact that at autopsy bile could be squeezed from the common duct, some bile must have made its way during life into the intestine. There was nothing to suggest hemochromatosis.

FIBRINOUS BRONCHITIS

December 16, 1918.

I AM not going to ask any one of you to go over this patient (Med. No. 9990) this morning because his physical examination is relatively unimportant. The patient is twenty-two years of age, and he comes in complaining of stomach trouble and breathlessness. His family history is entirely negative. There are no diseases in his family that would suggest any hereditary relationship to his condition. He is single. His habits are good. For three years he has been a helper to a plumber. For some years previous to that he drove a milk team and went to school. There has been no history of exposure to irritating fumes.

He was born in Portland, Maine, but moved in early childhood to Boston, where he has lived since. His general health has been good. He had chickenpox, mumps, and whooping-cough. There has been no exposure to tuberculosis and no history of acute infectious diseases beyond the three mentioned. In childhood he sustained a blow in his back, which he holds responsible for a partial paralysis and shortening of his right leg. He has not been subject to head colds and has had no discharge from his nose. He has had some obstruction in his nose which I I will refer to later. There is no history of tonsillitis, sore throats, hoarseness, or sore mouth. His cardiorespiratory history is negative.

He has always eaten generously of a wide variety of food, and has had an excellent appetite. His bowels have always been a little sluggish, so that once in two weeks he has had to take a cathartic. There has been no nausea, vomiting, gas, hematemesis, distress, colic, icterus, diarrhea, clay-colored, bloody, or tarry stools. No hemorrhoids. His genito-urinary history is entirely negative. His neuromuscular history is entirely negative. His best weight was 165 pounds six months ago. Recently he has weighed 127 pounds. His loss of weight has been entirely

during his present illness, which has been of three months' duration. His present illness began three months ago.

The patient was awakened three months ago by a severe cough and feeling of breathlessness. The cough was succeeded by the eructation of much gas, during which time his breathlessness and feeling of oppression grew steadily worse. After an hour the attack gradually passed and he went back to sleep. Each night since he has had similar attacks, increasing in frequency, duration, and severity. The attack almost invariably begins with a cough, which raises a varying amount of sputum, usually thick and greenish, occasionally white and frothy. The cough is followed by the distention with and eructation of large quantities of gas, which is succeeded by difficult and wheezy breathing. Expiration is much easier than inspiration. Often the only way to relieve his distress is to take up a position on his hands and knees. Toward the end of the attack vomiting frequently occurs. The vomitus is green and watery and never contains food.

He describes his sensation during the attack as though a hand were squeezing his windpipe, and the end of the attack comes when the hand gradually lets up. The attacks occur rarely in the daytime, although he is frequently wheezy and inclined to coughing spells. After meals is his most dangerous time of the day, but these attacks are less severe than the inevitable nocturnal attacks. The cough makes his head ache and often brings on vomiting. Two months ago his increasing weakness forced him to stop work. Five weeks ago he went to a local doctor, who discovered a polyp in his nose, and is said to have removed it. His nasal obstruction was partially relieved, but his attacks were no fewer.

About a month ago he went to a doctor in Portland, who gave him adrenalin hypodermically, and this relieved his attacks promptly. Every night since then he has had to have adrenalin sometimes several times during the night. It always gives him temporary relief, but he thinks he is apt to be more wheezy next day. He has vomited almost every day of the past fortnight, always after coughing. Solid food makes him so much worse

that for weeks he has lived on milk and milk-toast. Coughing gives him a severe headache and some epigastric pain. He also complains that a deep breath hurts his stomach. A few times severe coughing has led to faintness. He is increasingly constipated. He complains of a nasty taste in his mouth.

His physical examination, as I said, shows relatively little. In regard to his pulmonary condition, when he came in, this note was made: "Over the whole of both lungs, most marked near their bases, are heard multitudes of squeaks and groans, and occasional coarse moist râles. All are more marked on inspiration. Resonance is unimpaired. Tactile fremitus, voice, and breath sounds are quite normal. Lower borders of lung in back are low and move very slightly with forced respiration."

The morning after admission the physical examination was perfectly negative. Three or four days later I made this note on his lungs: "The lungs are slightly hyperresonant throughout. Expiration is distinctly prolonged and slightly high pitched. Apparently normal pulmonary condition."

Since he has been in the hospital he has run a little fever, the highest being just a trifle over 100° F. His respiration has not been particularly rapid. His pulse, at times, has been a little rapid. Practically every night he has had an "asthmatic" attack, and several times during the day he has been moderately dyspneic. In the first severe attack he had in the hospital the difficulty seemed to be inspiratory chiefly. Inspiration was quick and deep and expiration much prolonged and wheezing. Adrenalin relieves his attacks promptly, but makes him tremble and makes his eyes burn. A very mild attack, a day or two ago, was relieved, as it seemed, by a sterile hypodermic, but last night he had a very severe attack on which a sterile hypodermic had absolutely no effect, though his attack was relieved promptly by adrenalin.

On December 13th this note was made: "Patient's asthmatic attacks have continued, but are promptly relieved by adrenalin. He has had at least one attack every night since entry. He is running a slight temperature between normal and 100° F. Yesterday he was started on a saturated solution of potassium

iodid, 1 c.c. three times a day. Dr. Walker is giving him sputum vaccine."

DR. CHRISTIAN (to Patient): How about your attacks in the last two or three days?

PATIENT: I have only had one since Dr. Walker injected the serum.

DR. CHRISTIAN (to Patient): What day was that?

PATIENT: Last Thursday. (Clinic on Monday.)

DR. CHRISTIAN: On last Thursday he had an injection of "serum." A vaccine has been made from the organisms from his sputum, and he has had only one attack of dyspnea since that was given. Also he has been receiving a saturated solution of potassium iodid, 1 c.c. three times a day. Here is a specimen of his sputum which I will pass around. It happens that, since he has had this treatment, he has not had in his sputum what I am particularly anxious for you to see, namely, bronchial casts. He coughed up in his early stay in the hospital casts of his bronchi which showed branching, with various subdivisions going down into finer ramifications, the kind of thing that is shown in this picture that I will pass around [1] (Fig. 236). I think you can see it is simply a cast of the bronchial tree. Then his sputum has been of the watery character, a considerable amount of sputum, and in it floating masses, flocculent masses, and, when he coughs up these casts, they come up, as you might expect, in just such flocculent masses, but in the fluid they separate out and you can see the casts. Examined under the microscope the casts have the appearance of a homogeneous matrix in which are running fine fibrils or threads, and covering the casts or mixed in with the casts are a considerable number of leukocytes with rather coarse granules. These are eosinophilic cells.

(House-officer asked if any Charcot-Leyden crystals have been found in this case.)

ANSWER: No, none have been found.

DR. CHRISTIAN: None have been found in his sputum, so he has that type of sputum with these casts of his bronchi and with

[1] Illustration from Bettmann's paper, Amer. Jour. Med. Sci., 1902, cxxiii, 304.

eosinophilic cells. He has no eosinophilia in his circulating blood. His differential blood count is normal. He has moderate leukocytosis, 15,000 when he came in, which gradually dropped to 8100.

His pulmonary examination shows wheezing and at times bronchi. *x*-Ray plate shows no areas of consolidation, but shows rather a marked bronchial tree, rather more than we see in the average chest plate. You see it well marked here (indication to

FIG. 236.—Fibrinous bronchitis cast expectorated; three-fourths natural size (Milton Bettmann, in American Journal of the Medical Sciences).

plate), and you see the ramification going to the lower lobe and also to the upper lobe. Here is a small round dense area, possibly suggesting a small area of calcification. At the roots of the lungs on both sides there is a good deal of density, either thickening around the bronchi or some enlarged peribronchial lymph-nodes. There is no evidence in the plate of infiltration at the apex or anywhere running out to the periphery of the lungs; so,

as far as the process goes, it is suggestive of peribronchitis with possibly some dilatation of the bronchi, but that is not very evident. It is more a plate of peribronchitis than bronchiectasis. There is no deformity of the diaphragm and no signs of pleural thickening.

Occasionally in these cases you can get queer signs on auscultation described as flapping or crackling sounds due to the air being pushed by the cast in the bronchus, and the bronchus acting with the cast in it temporarily with a sort of valve-like action. All he shows this morning is the rather louder prolonged inspiration, and with expiration there is a certain amount of crackling sound, no particular amount of râles, and no real extraneous sounds. Sometimes when you get an extraneous sound it serves to locate what part of the pulmonary tissue the cast comes from. The effort has also been made to locate the origin of the cast as to whether it is from the upper or lower lobe, because casts from the upper lobe do not have as many or varying branches as those from the lower lobe, but that diagnosis would be possible only with large casts and pretty numerous ones.

This is distinctly an unusual condition. It is what is spoken of as fibrinous bronchitis, and Babcock in his book has given it the term "plastic bronchitis." The reason for calling it plastic bronchitis rather than fibrinous bronchitis is that, taking up the question of the structure of these casts, they often do not contain very much fibrin, some are nearly entirely made up of mucus, and in others there is a considerable amount of fibrin, but in most cases there is a mixture of both, and the term "plastic" does away with the difficulty of the term "fibrinous" when the thing is not made up of fibrin.

Here I want to read just briefly the history of two other cases to impress on your minds the characteristics. The following was a patient of Dr. Landis,[1] of Philadelphia: "The patient was a robust healthy male, aged forty-seven, referred to him because of suspected tuberculosis. The family history was negative and he had never had any illness. Four weeks prior to his coming

[1] "Diseases of the Chest and the Principles of Physical Diagnosis," Norris and Landis, W. B. Saunders Company, 1917, page 265.

under observation he had caught cold. The trouble started as a coryza, and in a few days had developed dyspnea. For the first two weeks the sputum, which was moderate in amount, was thick and whitish in color, later it had a greenish tinge." (Remember, our patient's description of the sputum was that it was whitish and sometimes greenish.) "On one occasion after a paroxysm of coughing he spat into his handkerchief a small hard pellet, which, on examination, proved to be a cast from one of the medium-sized bronchi. There was a slight elevation of temperature during that attack. The sputum was negative for tubercle bacilli, but contained both pneumococci and streptococci. With the exception of one day spent in bed he attended to his professional work, although with some effort. His appetite was good and he had lost no weight. On physical examination there was deficient expansion at the right base, impairment of the percussion note, suppressed breath sounds, both large and small râles, and, in addition, a flapping sound heard at the end of inspiration. The patient was sent to the seashore and, when seen two weeks later, there was nothing abnormal to be noted over the areas previously affected."

Another case is one reported by Dr. Bettmann in the American Journal of Medical Sciences for 1902, cxxiii, 304: "The patient was a negress aged twenty-two years, who came to the hospital on the obstetrical service. She gave a history that six years before, in the fall, she had an attack similar to the attack observed in the hospital, the symptoms being cough, pain, respiratory distress, profuse expectoration, containing, evidently from the patient's description, branching casts. Following this attack she had pneumonia and was confined to bed for one month. Every year in the fall since that time she has had similar attacks. These attacks had no relationship to her previous pregnancies, which occurred two and three years previous to entrance to the hospital, respectively. She has lost weight throughout the last two years." (Most of the rest refers to her pregnancy, which was normal, with a normal delivery, etc.)

"On the tenth day following her delivery she was allowed to sit up in a chair, but the discomfort from her cough increased so

much that she was put to bed again, her evening temperature having touched 102° F. On the thirteenth day of her puerperium I was in the ward delivering another case, and my attention was called by the nurse to the patient's extreme dyspnea." The description of the dyspnea is as follows: "The patient is sitting up in bed in intense dyspnea. All the accessory muscles of respiration are called into play. The alæ nasæ dilate with each respiratory movement. She coughs incessantly, and brings up large masses of expectoration. She is complaining of an intense sharp pain radiating from the lower left side through the back, increased on coughing. Respirations are 35 per minute; pulse 100; temperature 102° F. Loose tracheal râles are heard in the throat. On palpation there is normal vocal fremitus throughout. On percussion there is high tympany in both lower axillary regions, higher and approaching dull on the right. On auscultation over the front respiration is prolonged and accompanied by moist râles. The breathing is more intense in the right lower axilla, and approaches tubular breathing in its quality. The inspirations are here accompanied by râles distincly crepitant in character. The attack of dyspnea lasted about one hour. That attack was on September 25th.

"She had another attack not so severe in character on October 11th, eleven days later, and between those two attacks she had slight respiratory distress and her evening temperature ranged between 100° and 101° F. She had slight cough and occasionally expectorated small casts, which caused her very little discomfort. On one occasion a to-and-fro vibrating sound was heard on expiration in the right axilla. This corresponds in character to the 'ventilgerausch' of the Germans. The urine was negative throughout. The patient continued to have a slight cough and dyspnea and slight evening temperature, and left the hospital in spite of protests October 10th. She remained in Baltimore three weeks after her discharge from the hospital, and had frequent attacks of violent coughing and expectorated 'tree-like things,' according to the description of a friend. She then went to her home in Virginia, where she died two weeks later. No data as to the cause of her death were obtainable."

In this paper by Bettmann there is a very careful review of the literature and a classification of the cases, and he subdivides the cases into nine different groups: (1) Chronic bronchitis with expectoration of branching casts of the bronchial tree, 27 cases. Those are all the cases he could find reported in the literature up to 1902. That is what happened, judging from the description, in his case and also in the case of Dr. Landis, and they very closely resemble our case. I should call it chronic bronchitis with expectoration of branching casts of the bronchial tree. (2) Acute bronchitis with expectoration of branching casts of the bronchial tree, 15 cases. In those acute cases the attacks come on more suddenly, are of shorter duration, and are accompanied by a higher range of temperature. In those cases the temperature sometimes goes up to 104° F.; in other words, it is more like acute bronchitis, but it is rather difficult, I should think, in classifying them to say just which cases go into one group and which in the other, that is, they shade into each other. (3) Six cases in which no casts were found during life, but were an accidental finding after death. (4) Cases in which the casts expectorated showed no dichotomous branching, 11 in the literature. (5) Expectoration of branching casts in organic heart disease, 10. (6) Expectoration of branching casts in pulmonary tuberculosis, 14. (7) Expectoration of small casts, often non-branching, in association with asthma, 5. (8) Formation of casts in the bronchi in association with pulmonary edema following thoracentesis, 4. (9) Cases whose classification is doubtful because of incomplete reports, 6. You see the total number of cases from the literature is a relatively small one. The association with tuberculosis is of interest. This case of Dr. Landis was sent to him with the probable diagnosis of tuberculosis, but he could not find any evidence that there was tuberculosis. Dr. Landis says that he has seen no evidence of bronchial casts in the ward patients in the Phipps Institute, which is a tuberculosis hospital, over a period of thirteen years (he is Physician-in-Chief to the hospital), nor have such casts ever been found in any of the 662 autopsies on tuberculous patients, which brings out the probability that the finding of the condition in a patient with tuberculosis is simply a coincidence. It just

happens to occur in a case of tuberculosis. The other point of view is that the tubercular lesion is responsible. The same remark is applicable to the finding of the casts in chronic heart disease. It may be that it is simply an accidental association and not a causal relation.

In regard to the association with asthma, it brings up the question as to whether, after all, it is not a mistaken diagnosis to call these cases of bronchial asthma. We have had under observation here somewhere between 400 and 500 cases of bronchial asthma, and this is the first patient with a history suggestive of asthma in which we found these casts. Of course, Curschmann spirals, of large enough size to be picked out macroscopically, are very common in asthma, but Dr. Walker has never seen these branching casts in his asthmatics, and both Dr. Walker and myself remarked on seeing this history that it was not the history of an asthmatic. This patient has a different kind of dyspnea. The difficulty is in inspiration rather than expiration, and asthmatics do not get on their hands and knees to relieve their dyspnea; they go and sit by an open window. The asthmatic very often, with his paroxysms of asthma, has an associated gaseous distention of his stomach, probably due to the swallowing of air during his asthmatic attack. Is it not uncommon for the typical asthmatic to come in complaining of his stomach, and to tell you that, accompanying or following an asthma paroxysm, he belches up a large amount of gas, and very frequently they say that they relieved their asthma attack by the belching of gas. Some say they have indigestion and gaseous distention preceding the asthmatic attack, so that phase of the thing in this patient is not different from asthma. Very often the asthmatic attack with strain, etc., does lead to vomiting, but, taking the story of this patient's attacks as a whole, it is not the definite picture of asthma. Dr. Walker made a note the day after the patient came in, "No evidence of bronchial asthma in this case at the present time."

The etiology of the condition is quite obscure. There are one or two postmortem observations that show no definite lesions in the lungs. In cases where the casts have been found, the

bronchi may show a break in the continuity of the epithelium. In other cases the bronchial epithelium has been seen to show large numbers of mucus-secreting cells, and they have been very prominent, as if there was an exaggerated secretion from the normal mucous glands of the bronchial mucosa.

The structure of the casts have been studied in various cases. I will pass this article of Dr. Bettman (loc. cit.) around because there is a picture on page 306 of the microscopic appearance of a section of one of these casts, and on page 309 there is a macroscopic drawing of a cross-section of a large cast. The structure in the larger portion is partly tubular, that is, the cast does not fill the larger bronchus with a solid mass, but is like a deposit on the surface of the mucous membrane of varying thickness, and so the central part is incomplete. In other words, it is a tubular cast rather than a solid one. If you study that a little more carefully, you will find that, instead of being on cross-section simply a more or less circular mass with a smooth inner wall, you will find that inside the outer layer are whirls and masses of various size as represented in that picture. This suggests the mechanism of formation of a cast as being formed in the smaller bronchi, and then, by coughing, being loosened and pushed up a certain distance; while this is going on the mucous membrane continues to secrete mucus which forms the peripheral part around the central part, made up of irregular whirls and masses which, as they are formed, have been pushed up. When you get down into the smaller bronchi the cast is solid, and under the microscope you will notice a mucous or gelatinous matrix, and in it fine fibrils that run in various directions, sometimes interlacing. If that is stained by methods that demonstrate fibrin you find that a certain number of these threads, varying in different cases, will take the fibrin stain, the ordinary Weigert fibrin stain, which shows that some of the fibrils by staining reaction are fibrin. In other words, the matrix seems to be made up of mucin, it gives the staining reaction of mucin in which are fibrils, some of which may be fibrin.

There is an intestinal condition which in many ways is very similar to fibrinous bronchitis. This intestinal condition is

pretty common, but fibrinous bronchitis is pretty uncommon. That intestinal condition is what you are probably very familiar with as mucous colitis. It is a condition in which the patient passes casts of the intestinal tract, largely of the lower part of the colon, often tubular, and rather apt to be bile stained; otherwise they have the same general appearance as the casts that this patient coughs up. If you look at the intestinal casts under the microscope, you see they are made up of mucus, and in that mucus runs a certain number of fine threads or fibrillæ, and, if stained, you find that it is partly mucin in reaction and partly fibrin. Mixed in with the casts you find a certain number of cellular elements which in the intestinal casts are usually lymphocytes, red blood-cells, and a certain number of desquamated epithelial cells.

Mucous colitis is a condition which has just the same indefinite etiology as this so-called fibrinous or plastic bronchitis. In both conditions there is, in most cases, an element of neurosis; they are apt to occur in people of rather unstable neurotic make-up, people of the type with rather active reflexes, etc. The same thing you know is true of asthma. A great many of the asthmatics have this indefinite neurotic element.

In the case of fibrinous bronchitis usually you find mingled in with the casts, more on the surface than inside, varying kinds of bacteria, and cultures made from the sputum will show a flora, which, after all, is not very different from the flora that you get in various forms of chronic bronchitis and which you get in asthma. This particular patient's culture showed a hemolytic streptococcus and Streptococcus viridans, and from his sputum culture a vaccine has been made, and we have been using that in treating the case.

Probably what has happened in this patient is that he developed some form of bronchitis which is persistent in character, not very severe in nature, and along with that from time to time has occurred the formation of these casts, and his very violent spells of coughing have been at times when these casts were rather extensive and vigorous coughing is necessary to expel them. Running along through the whole thing has been per-

sistent bronchitis. You heard him coughing since he has been in here, a certain wheezing cough with a little rattle to it, just the kind of cough the asthmatic has between asthmatic attacks.

In this condition esosinophilic cells are a common finding in the sputum, free and attached to Curschmann spirals, and this man's sputum shows a considerable number of these eosinophilic cells, but no spirals. In the descriptions of the casts very often it is said that the terminal portion of the cast is of the structure of a Curschmann spiral. In that picture passing around you see at the tip of the cast a very fine terminal structure which shows a tendency to be twisted on itself. The Curschmann spiral you know has a mucous matrix with one or two threads of more highly refractive material running in it, and the whole thing is twisted on itself, hence the name spiral; so very often these casts are described as showing Curschmann spirals at the tip of the branches.

It is not at all unlikely that there will be some relief from the condition following the use of the vaccine very much in the same way that we often see improvement in chronic bronchitis and asthma from a vaccine made of the predominating organism in the sputum. The therapeutic effect of adrenalin which is quite striking in this case is quite similar to the therapeutic effect of adrenalin in asthma, probably due to the same reason, namely, wheezing and difficulty in breathing is from bronchial spasm and that is relieved by adrenalin. In this particular case it may be of the nature of an ordinary asthmatic attack or simply may be a reflex spasm from the local irritation of the cast material which occupies the bronchus. If you have ever inspired a crumb you know the kind of a violent cough it will lead to, and when the coughing keeps up you are apt to go into this wheezing type of dyspnea. That is undoubtedly due to reflex spasm because ordinarily when one inspires a crumb it does not go very far down into the bronchial tree, it goes down a certain distance, but the dyspnea is largely a reflex affair.

It was described in this case that when he first came in the diaphragm apparently moved very little, that is, the excursion at the base of the lungs was very slight. We find that in various

kinds of spasmodic breathing, often very commonly in the cases of asthma, so that with the patient in front of the fluoroscope, when having the asthmatic attack, you can see that the lungs are blown up on account of the difficulty in expiration, and you can see that the diaphragm has a low position, and that with each inspiration the motion of the diaphragm is very slight. With the patient in front of the fluoroscope, if you will give him a subcutaneous injection of adrenalin, the dyspnea will be relieved, and the change that you can see take place is an increase in expiration, and an increase in the density of the lung, while the diaphragm has a more evident motion; gradually there is wider and wider excursions, until you get normal movement of the diaphragm, and from being a flattened diaphragm it becomes changed to a normal dome-shaped diaphragm at a higher level. That is the effect of the adrenalin. Very likely in this case the adrenalin has very much that therapeutic effect. The striking thing in this history has been the fact that adrenalin relieved the attacks of dyspnea promptly, but did not have much effect on the underlying condition. The dyspnea kept up just the same as far as recurring attacks were concerned, and it seemed to him as if he wheezed a little more throughout the next day after the attack was relieved. That is the same sort of thing that you find quite frequently in asthma.

Whether the injection of the vaccine with the use of the potassium iodid has made this striking change in the patient, or whether it is an effect of change in environment I do not think that you can say. It does not follow because of his relief immediately following a certain therapeutic measure that the therapeutic measure has produced that relief. The history of this condition is one of attacks lasting, as this one has, for several months, then gradually subsiding and leaving normal respiration. In some patients the attacks occur but once, and do not recur. In other cases they recur, such as in the negress whose history I gave you, who apparently every autumn for some time had been having these attacks. In other cases an irregular recurrence takes place over a number of years, so it may be that three months of attacks is about the length he is going to have, and the thera-

peutic measure really has not been effective. On the other hand, knowing of the results we have gotten in chronic bronchitis and asthma with sputum vaccine, that seems the rational form of therapeutics to carry out, and the response would seem presumptively one of cause and effect, a result of treatment. Of course, the idea of potassium iodid is to increase somewhat the bronchial secretion, really to have a larger amount of serous mixture, and probably dilute the mucus enough to prevent the formation of the casts, or anyhow to have more liquid and have the casts less closely applied to the mucus membrane and consequently more easily raised by coughing.

Apart from this condition the patient is normal. There is no evidence of any cardiac lesion, no evidence of any respiratory lesion beyond this, no evidence of any tuberculosis, and no evidence of any renal lesion. The blood-pressure is a little below normal rather than above normal, and between attacks he has a slight suggestion of chronic bronchitis, and with the attacks he has this dyspnea.

We have seen in this clinic a great many cases of cardiac disease with nocturnal dyspnea, but we do not find in those cases the type of sputum such as is being passed around, quite abundant sputum with casts in it. We have never seen the casts in any previous case. It is fair to say that they might be easily overlooked unless the sputum were examined macroscopically. There is an unfortunate tendency among students and house-officers to look at everything with the microscope and not look at it with the naked eye. It is like the proverb in the Bible of the mote and the beam, the very important beam is very often overlooked and the insignificant mote is carefully described, so I should not like to say we have not had any cases with casts in the sputum, but I can say that nobody has found any casts. Dr. Walker has been examining his asthmatics rather more carefully in regard to sputum, etc., and I think his figures are more reliable than the figures from our records, and he has not seen any of these casts.

A great deal can be learned from the sputum by doing two things which are relatively infrequently done, one is measuring

the sputum and knowing how much sputum a patient raises, whether it is increasing or decreasing. That ought to be done in all cases where there is chronic bronchitis, and especially bronchiectasis, because the variation when there are large cavities is a striking thing. The sputum is rarely measured, so the average student has very little idea as to whether the twenty-four-hour sputum should be 10 c.c. or 10 liters. You would be quite surprised often, I think, to find how much sputum a patient, who does not seem to cough very often or raise very much at a time, succeeds in bringing up in twenty-four hours. The other thing I have already referred to, and that is the macroscopic examination which tells you about bacteria to a certain extent from the smell and from the color of the sputum. Observation of the amount, color, and odor of sputum gives you a great deal of information. The odor is very important, and yet I doubt if anybody smelled that specimen as it went around to see whether it had an odor or not. Does anyone know what it smells like?

STUDENT: It has a certain aromatic smell.

DR. CHRISTIAN: What is that due to?

STUDENT: Probably medicine.

DR. CHRISTIAN: That medicine might have been put in the patient or put in the sputum. What does it smell like?

STUDENT: Like some coal-tar product.

DR. CHRISTIAN: Yes, it smells like some sort of thing that was put in there to keep it sweet and preserve it. It is certainly not a foul smell such as you often get from a case of bronchiectasis or lung abscess. If we have any sputa of that variety I will bring it in and let you smell it. It is an entirely different proposition.

You see from the odor of that sputum and the fact that there is very little odor to it, there is presumptive evidence that this patient has not any dilated bronchi in which the liquid material accumulates for a long time and is mixed with bacteria that causes putrefactive changes. That is what you get in bronchiectasis. This sputum, though abundant, is suggestive of the odor of sputum that comes from a condition not having much dilatation of the bronchi.

Examination by *x*-ray gives this picture, which probably represents more peribronchial thickening than dilatation of the bronchi. Of course from the *x*-ray picture you cannot tell whether a shadow running down, such as this, is due to thin-walled dilated bronchi or due to normal bronchi, as far as the bore of the tube is concerned, with thickened wall.

The important thing in this patient is the future as to whether he is going to have a recurrence of the condition or not and the best way to prevent that probability. I am inclined to think that a patient with this sort of history should live very much the out-of-door life of the case of tuberculosis that is well enough to be at work. That is, he ought to sleep with his windows wide open and get as much fresh air as possible and ought to be overnourished. There is no indication for him to keep at rest if the paroxysms of dyspnea do not interfere with his work. I think it is decidedly advisable for him to have a course of vaccine treatment on the basis that there may be an underlying chronic bronchitis of bacterial origin, and the vaccine will possibly decrease that, and so decrease the occurrence of these paroxysms of dyspnea due to the accumulation of these casts. With that sort of general hygiene he may remain entirely free from these attacks the rest of his life.

One etiologic factor I referred to in giving his history, saying there was no exposure to irritating fumes. Some of the cases of acute fibrinous bronchitis have followed acrid fumes, such as ammonia fumes or the gas that comes from a fire, where the patient has inspired the smoke and gas in a burning building. Then there is a condition which is a terminal process following the inspiration of these irritating gases, which is spoken of as bronchiolitis fibrosa obliterans, where the gases have led to inflammation in the finer terminal bronchioles with subsequent connective tissue formation in the wall and obstruction of the fine terminal bronchi. That is an extremely rare condition, but it is well enough to keep it in mind in connection with this other condition which is relatively a rare one.

CLINIC OF DR. JOHN LOVETT MORSE

CHILDREN'S HOSPITAL

INFANTILE SCURVY

January 17, 1919.

THIS baby, who is nine months old, comes to the hospital from one of the larger cities of Canada. His father was told by several physicians there, including an eye specialist, that the baby's condition was incurable. His family physician told him that it was useless for him to take the baby to Boston, but, as the baby's mother would never be satisfied if he was not taken there, it would be best for him to go.

The parents are well. There are no other living children. One child died at twenty months of some disturbance of the digestion. There have been no miscarriages.

He was born at full term after a normal labor, was normal at birth, and weighed 5 pounds and 11 ounces. He was nursed for six months. He was then fed on pasteurized cow's milk, modified according to the formulæ given by the proprietors of Phillips' Milk of Magnesia. The present mixture is made up of the

Top 9 ounces of a quart of milk.
9 ounces of barley-water.
1 ounce of milk of magnesia.
1 ounce of milk sugar.

The milk is still pasteurized. This mixture contains about 5.50 per cent. of fat, 7 per cent. of milk sugar, 1.50 per cent. of protein, and 0.75 per cent. of starch. He has been taking five feedings of 8 ounces at four hour intervals. He has not vomited and has had one or two normal stools daily.

It has been rather difficult to get accurate data as to the

sequence of events, the mother, the aunt, the trained nurse, and the nursery-maid all giving different dates. As far as I can make out, however, it was noticed about six weeks ago that he cried when his diapers were changed and when he was given his bath. A little later he acted as if his back was tender, and recently his legs have been tender when they were touched. Little attention had been paid to the tenderness in the legs and back, however, because of the more marked symptoms in the eyes. Three weeks ago his left eye began to bulge, and within fifteen or twenty minutes was very prominent. A large ecchymosis appeared shortly afterward in the left upper lid. Ten days later the right eye also protruded, and an ecchymosis appeared in the right upper lid. He had a slight nosebleed at the time when the right eye swelled. A discoloration was noticed in the roof of the mouth at about the same time. The color of the urine has not been noted.

Physical Examination.—He is fairly developed and nourished, but markedly pale. The anterior fontanel is 3 cm. in diameter and level. The head is of good shape. Both eyes are, as you see, very prominent, so prominent that he cannot quite close the lids. The conjunctivæ are, however, not inflamed. There is no limitation of the motions of the eyeballs. The pupils are small, but react quickly to light. Both upper lids are stained bluish-brown and the lids are a little puffy. He sees well, and there is no trouble with his hearing. There are no teeth, and the gums are healthy. The tongue is clean. There is an ecchymosis about 3 cm. long and 2 cm. wide on the posterior part of the hard palate in the median line. There is a moderate rosary, but the chest is of good shape. The right border of the cardiac dulness extends 2½ cm. to the right, and the left 6½ cm. to the left of the median line. That is, the heart is slightly enlarged to the right. The action is regular. The rate is 160. There is a slight systolic murmur at the pulmonic area. The second sound at the pulmonic area is normal. There is also a slight systolic blow in both sides of the neck. The lungs are normal. The level of the abdomen is that of the thorax. Nothing abnormal can be detected in it. The lower border of

the liver is palpable, 1 cm. below the costal border in the nipple line. The spleen is not palpable. He uses his arms freely and, as you see, they are not tender. There is, however, some swelling over the lower portion of the diaphysis of the radius on each side. This swelling is deep down and is slightly tender. It is not, however, red or hot, and does not pit on pressure. When I prick his feet with a pin he draws his legs up, as you see, but shows by his actions that he would prefer not to move them and that it hurts him to move them. There is, nevertheless, no limitation to passive motions at any of the joints. There is a little swelling about the shaft of the right femur. This swelling is very tender, but is not red or hot, and does not pit on pressure. There is some swelling about the lower portions of the shafts of the tibiæ and fibulæ on both sides. These swellings are also tender, but not red or hot. They do not involve the epiphyses or the joints. The knee-jerks are equal and unusually lively. Kernig's sign is absent on both sides. There is no enlargement of the peripheral lymph-nodes. The rectal temperature is 102° F. The pulse is 160. The respiration is 60.

The urine is light red in color, turbid, acid in reaction, and of a specific gravity of 1022. It contains a very slight trace of albumin, but no sugar. There is 1 cm. of sediment in the centrifuge tube. This contains many red blood corpuscles and a few white corpuscles, but no other cells or casts.

The stool contains a slight excess of soap, but is otherwise normal. The guaiac test for occult blood is negative.

The hemoglobin by the Sahli test is 45 per cent. The red corpuscles number 3,500,000, and the white corpuscles, 18,000. The red corpuscles show some achromia and anisocytosis, but no polychromatophilia, poikilocytosis, or nucleated forms. The differential count of the white cells shows:

Mononuclears	60 per cent.
Polynuclear neutrophils	39 "
Eosinophils	1 "

Diagnosis.—I am sure that you have all already made the correct diagnosis, because I know that you are familiar with this

disease. You are all, I am sure, also congratulating yourselves upon being so much brighter than the physicians in the Canadian city. You must not feel too much pleased with yourselves, however, because ten years from now, when you are not in touch with large hospital clinics and when you have not seen one of these cases for a good many years, more than half of you will fail to recognize it. To one who is familiar with this disease there can be, of course, no differential diagnosis in this instance, because there is no other disease but scurvy which gives these characteristic symptoms and physical signs. The tenderness of the legs and back on handling and the peculiar situation and characteristics of the swellings about the bones of the extremities are absolutely pathognomonic. The blood in the urine, without casts or cells, is also characteristic of the hematuria of scurvy and inconsistent with acute nephritis. The sudden protrusion of the eyes could only be caused by a hemorrhage into the orbit. No new growth could have forced the eyes forward so quickly. Furthermore, if the protrusion of the eyeballs was due to an increase in the intracranial pressure, there would be also bulging of the anterior fontanel and evidences of cerebral irritation. The ecchymoses in the eyelids are also corroborative of this etiology, as is the bleeding from the nose at the time of the protrusion of the right eye. The ecchymosis in the roof of the mouth is also corroborative evidence of scurvy. There would be, in all probability, swelling and discoloration of the gums if there were any teeth. Further, but less important, evidences of scurvy are the anemia, the slight enlargement of the heart, the rapidity of the pulse and respiration, and the exaggeration of the knee-jerks. The murmur at the pulmonic area and the systolic blow in the neck are unquestionably functional in character and of no importance. The elevation of the temperature is not inconsistent with scurvy, although many of the text-books give the impression that uncomplicated scurvy is never accompanied by fever. I have, however, seen it very frequently.

The most interesting feature in this case is that the hemorrhages into the orbits have been so large, when the other signs of scurvy have been so mild. It is also interesting to note that

the signs of rickets are so slight, although the scurvy is so marked. The mixture being a perfectly rational one, the cause of the scurvy in this instance is almost certainly the long-continued use of the pasteurized milk.

Prognosis.—The prognosis is absolutely good with proper treatment. The temperature will drop to normal within a few days and the blood will also disappear from the urine. The tenderness in the back and extremities will probably all be gone within a week. The eyes will quickly begin to go back into their normal position, but it will probably be two or three weeks before they will be quite where they belong. It will take some time, of course, for the ecchymoses in the eyelids and in the roof of the mouth to disappear.

Treatment.—The treatment is very simple, namely, 2 tablespoonfuls of orange juice once daily. This should all be given at one time one hour before some feeding. It may be given plain or diluted with water. If the baby dislikes it, it may be sweetened with a little granulated sugar.

The baby will recover, even if the pasteurized milk is continued. There seems to be no reason for continuing it, however, because a clean and safe milk can be provided for the baby. It is apparently digesting very well the mixture which it is taking. It seems irrational, however, to be giving a baby so much magnesia, and the stool shows that the baby is not quite taking care of the fat in its food. We will give it a mixture containing 3 per cent. of fat, 7 per cent. of milk sugar, and 1.50 per cent. of protein, adding 2 grains of citrate of soda to each ounce of milk and cream in the mixture to take the place of the milk of magnesia in facilitating the digestion of the casein. We will give the baby five feedings of 8 ounces at four hour intervals.

DISCUSSION OF INFANTILE SCURVY

Symptomatology.—Using this case as a text, I now want to tell you something of this disease as it occurs in infancy. The earliest symptoms of infantile scurvy are pallor, edema of the eyelids, especially of the upper, loss of appetite, disturbance of the growth and nutrition, and cardiorespiratory disturbances.

There is nothing characteristic about these symptoms, which may occur, of course, in many other conditions, except, perhaps, the cardiac-respiratory disturbances. Even these may also be due to other causes. The occurrence of any of these symptoms should, nevertheless, always suggest the possibility that scurvy is developing. The only way to determine whether these symptoms are due to scurvy or to some other cause is by the therapeutic test. If they are due to scurvy, there will be an immediate improvement when orange juice is given. It is very surprising, unless one is familiar with it, to see how rapidly the appetite will improve when orange juice is added to the diet, and how a baby, whose weight has been stationary for weeks, will begin to gain at once when orange juice is taken.

After a time the characteristic symptoms of scurvy develop. These may be divided clinically into three rather definite types. Usually, for a time, at least, the symptoms are entirely of one type, but in the well-developed cases the symptoms of all types may be present together.

In the ordinary type the first symptoms noticed are tenderness of the legs and back when the baby is handled. This is usually first noticed when the diapers are changed or the baby is bathed. The tenderness becomes more marked and the baby uses its legs less and less, finally not moving them at all unless compelled. Tenderness and pain on motion may also appear in the arms. After a time swelling appears about the long bones of the legs or of the arms. This swelling is due to hemorrhage between the bone of the shaft and the periosteum, and is limited, therefore, to the diaphysis. The swelling is tender and tense, but is not hot or red, and does not fluctuate. It does not involve the epiphysis or the joint unless, as happens in some of the severer cases, the hemorrhage has broken through the periosteum and into the tissues about. This swelling occurs most often about the femur, but is not uncommon about the lower parts of the tibiæ and fibulæ. It occurs more often in the forearms than in the upper arms. It is almost always bilateral. The position of the child is most characteristic. It lies on its back with its thighs flexed on the body and rotated outward, and with the

knees flexed on the thighs, that is, in the position which produces the least muscular strain, and is, therefore, the most comfortable. This position is fairly well shown in Fig. 237.

The baby does not move its legs. This is not because it cannot move them, but because it hurts it to move them. The legs are, therefore, held rigidly and are not flaccid. Passive motions at the joints are not limited except in the most severe cases. The knee-jerks are normal or exaggerated, and there is no disturbance of the sensation.

In the second type, the first symptom is swelling and discoloration of the gums about the teeth. The swelling is soft and

FIG. 237.—Position of legs in scurvy.

spongy, and the color purple. It occurs most often about the incisor teeth. It usually appears first and is most marked about the upper teeth. It may be present behind the teeth and not in front. Swelling and discoloration of the gums almost never develops unless the teeth have erupted, but does sometimes, however, when no teeth are visible.

In the third type the first and, often for a considerable length of time, the only symptom is the presence of fresh blood in the urine. In these cases the urine is red and contains albumin, but shows no casts or renal elements. There are no urinary symptoms except the discoloration of the urine.

In addition to these symptoms, which, as I have said, may all be present at the same time in advanced cases, there are other symptoms which are important, but less characteristic. Hemorrhages are the most common of these symptoms. They may occur anywhere in the skin, making ecchymoses of various sizes. Hemorrhages may also take place into the orbits, as happened in the baby that we have just seen. Bleeding from the nose or into the conjunctivæ is not uncommon. Cerebral hemorrhages, hemorrhages into the joints and hemorrhages from the bowels are, however, most uncommon. The pallor, which has been mentioned among the early symptoms, is always a marked symptom in the well-developed cases. Edema is also a not uncommon symptom of scurvy. This may occur in the eyelids, as already mentioned, or in the face or dependent portions. In addition to this ordinary type of edema there is also a very firm type of edema which occurs about the bones, especially of the lower legs. This type of edema does not pit on pressure and may easily be mistaken for hemorrhage about the bones. It is often a very confusing condition, and sometimes, if its real nature is not recognized, obscures the diagnosis.

Fever, even as high as 104° or 105° F., is not at all uncommon in the acute cases, although many of the text-books state that fever does not occur in infantile scurvy. I am sure that it does, however, because I have so many times seen a high temperature in scurvy without anything to account for it except the scurvy, and have then seen this temperature drop to normal in a few days, with the subsidence of the symptoms of scurvy under suitable treatment.

Certain evidences of neuritis, such as exaggeration of the knee-jerks and edema of the optic disks, are present in some instances. Enlargement of the heart, especially to the right, is not infrequent. An increase in the rate of the pulse and the respiration, especially of the pulse, is also not uncommon. The baby that we have seen today shows many of these minor signs, that is, exaggeration of the knee-jerks, enlargement of the heart to the right, and increase in the rate of the pulse and respiration.

Pathology.—I do not wish to take up the pathology of scurvy in detail. There is anemia in all cases. This anemia is of the secondary type, and shows the peculiarities of anemia of this type in infancy. That is, there is a tendency toward the chlorotic type of blood, to leukocytosis, and in the severe cases to reversion to a younger type of blood. The hemorrhages about the bones and their characteristics I have already spoken of. The bones themselves show some rather characteristic changes. The bone-marrow loses its lymphoid character and is poor in

FIG. 238.—Small hemorrhage beneath periosteum.

cells. It contains relatively few blood-vessels. There is much calcified ground substance, but it is not converted into true bone. The cortex of the bone is thinner and more brittle than normal. The density of the bone is diminished at the epiphyseal line. Fractures and separation of the epiphyses occur, therefore, more readily. The periosteum of the long bones is thickened and congested. The hemorrhages occur as the result of this congestion. In many instances there are also hemorrhages in the bone-marrow. These radiographs (Figs. 238–240) show some of these changes.

It is presumable that there are certain changes in the nervous system because of the exaggeration of the reflexes and the changes which have been found in the optic disks. These changes have, however, never been carefully studied.

The cause of the hemorrhages is still somewhat doubtful. The blood shows a slight diminution in clotting power. This diminution is not due to a deficiency of calcium nor to an increase in the antithrombin. The blood-platelets are normal. The

FIG. 239.—Large hemorrhage beneath periosteum with slight displacement of epiphyses.

changes in the blood do not seem, therefore, sufficient to account for the hemorrhages. Hess believes, from the use of what he calls the "capillary resistance test," that the tendency to hemorrhage is due to changes in the vessel walls and not to the blood. In this test he used a blood-pressure band to determine at what point petechial hemorrhages occur into the skin. Normal infants withstood 90 degrees of pressure for three minutes, but the vessels of infants with scurvy gave way under this pressure. This test is, however, not specific for scurvy.

Etiology.—There is not time for us to go very deeply into the various theories as to the etiology of infantile scurvy. It is most common in the second six months of life, presumably because so many babies get breast milk during the first few months of life and because after they are a year old they begin to get a more general diet. Sex plays no part in its production. We know furthermore that it is not due to improper hygenic

FIG. 240.—Large hemorrhage beneath periosteum with considerable displacement of epiphyses.

surroundings, to congenital or inherited debility, to other diseases, whether or not of nutrition, or to inanition or starvation.

Experiments on animals show that it is not due to starvation or to the long-continued use of a single article of food. They suggest that it is due to the lack of some substance in the food which is destroyed by heating or drying.

Clinically, it occurs very rarely in the breast fed, but may develop on any or all kinds of food. The conclusions of the American Pediatric Society, after its investigation on infantile

scurvy in 1898, were that "the development of the disease follows in each case the continued employment of some diet unsuitable to the individual child" and that "the farther a food is removed in character from the natural food of the child, the more likely its use is to be followed by the development of scurvy." In spite of the vast amount of experimental work which has been done since this time, no more positive conclusions are really justifiable now than when these conclusions were made twenty years ago. In my own experience, the most constant of the factors which may have been of etiologic significance has been the continued heating of the food. Clinically, the disease is easily cured by the addition of certain things to the diet, such as fruit juices and potato. Furthermore, when scurvy develops in babies that are taking heated milk, recovery takes place when the heating of the milk is stopped. All of these things seem to show pretty definitely that infantile scurvy is not due to the presence of some abnormal element in the food, but to the lack of some essential element.

It seems reasonable to believe that the element lacking is one of the so-called "vitamins," and that scurvy is one of the "deficiency diseases," belonging in the class with beriberi, pellagra, and perhaps rickets. The vitamins are sensitive to heat. This fact would explain the effect of heating the milk in the causation of scurvy. When, however, it develops in babies that are taking raw milk, we have to assume that there is a deficiency in the vitamins. Such a deficiency is possible, because it has been found that the amount of the vitamins in milk varies with the food and the nutrition of the animal, whether it be cow or woman. This fact will explain the occasional development of scurvy in breast-fed infants. The lack of growth in length, the evidences of neuritis, the edema, and the cardio-respiratory disturbances are also suggestive of the other deficiency diseases, especially beriberi.

A great deal of experimental work as to the etiology of scurvy has been done in animals during the past three or four years. The results of these experiments are somewhat conflicting. The conclusions which have been drawn from many of them are

probably erroneous, in that the experimenters have failed to realize that conclusions cannot be drawn from one species of animals and applied to another species, or from animals and applied to infants. The theory, which gained considerable credence about two years ago, that scurvy is due to stagnation in the colon with the absorption of toxins or bacteria, has been apparently disproved by more recent experiments. So also has the idea that the action of orange juice and lemon juice in scurvy is simply laxative rather than specific.

Diagnosis.—The diagnosis of scurvy is impossible in the early stages before the development of the characteristic symptoms. It should, however, as I have already said, be suspected when babies become pale, have edema of the eyelids, lose their appetite, cease to gain in weight and length, or have a rapid pulse and respiration. When these symptoms occur and there is no other obvious cause for them scurvy should be suspected, and the treatment for scurvy instituted. If scurvy is the cause of the symptoms, they will be quickly relieved.

Anyone who is familiar with the type of scurvy, beginning with pain and later showing swelling of the extremities, will never mistake it for anything else. Those who are not familiar with this type, however, make various other diagnoses, such as rheumatism, periosteitis, osteomyelitis, sarcoma, hip disease, Pott's disease, injuries, infantile paralysis, and multiple neuritis. Such mistakes ought not to be made. Rheumatism does not occur in infancy. If it did, and there were any swellings, the swellings would be about the joints and not about the bones. There would be heat and there would be redness. Periosteitis and osteomyelitis are serious, acute diseases. Babies with them are manifestly seriously ill. The trouble is usually limited to one bone or one extremity. Tenderness is sharply localized. If there is swelling, it is usually red and hot. The temperature is usually higher and more irregular. There is a marked leukocytosis. Sarcoma occurs in only one bone of one extremity. The swelling is usually not tender and is usually very hard. There is usually no fever and there are no other signs of scurvy. Hip disease is unilateral, there is limitation of motion at the

hip, the tenderness is over the joint, and swelling, if it occurs, is about the joint. In Pott's disease there is rigidity of the spine and usually an angular deformity. Psoas contraction is usually present. There are no other evidences of scurvy. Injuries are usually unilateral, sharply localized, acute, and there are no other signs of scurvy. Infantile paralysis is an acute disease. The lack of use of the extremities is due to paralysis and not to pain. The extremities are flaccid and are not held rigidily. There is no swelling. The reflexes are diminished or absent. Multiple neuritis is not a disease of infancy. The loss of use is due to paralysis and not to pain. There is, therefore, flaccidity, not rigidity. There is no swelling. The reflexes are diminished or absent. Many other minor points might be given in the differential diagnosis between scurvy and these other conditions. The points, which I have given you, however, are sufficient to prevent mistakes.

The type with swollen gums is often mistaken for difficult dentition. This mistake should never be made. The swelling of the gums in scurvy almost invariably occurs about teeth which have erupted, or are in process of eruption. The swelling in difficult dentition occurs above a tooth which has not erupted. The swelling in scurvy is purple and soft. The swelling in difficult dentition is red and hard. The eruption of the tooth relieves the symptoms in difficult dentition. The eruption of a tooth in scurvy has no influence on the symptoms.

The type of scurvy beginning with hematuria is almost never recognized. It is mistaken for nephritis, or the hematuria is attributed to stone in the urinary passages, tuberculosis or sarcoma. Sarcoma of the kidney, it is true, is sometimes associated with hematuria. The hematuria is, however, slight and intermittent, not marked and continuous. There is, moreover, almost always a palpable tumor in the region of the kidney if there is hematuria. Tuberculosis of the kidney and bladder in infancy is a pathologic curiosity. Hematuria almost never occurs in it. The urine, if it shows anything abnormal, contains pus. Stone in the urinary passages is also most unusual, although irritation of the urinary passages from crystals with

hematuria as the result sometimes occurs. In such cases the crystals can be found in the urine. If there is any doubt, the administration of an antiscorbutic will clear up the diagnosis in a few days. When there is a nephritis, there are always casts and other renal elements in the urine. These are, however, almost never present in scurvy, or, if present, there are very few of them.

Prognosis.—The prognosis in infantile scurvy is good. Recovery is rapid and complete under proper treatment. Hematuria usually ceases inside of a week. Tenderness of the extremities is usually gone in a few days. The swelling, however, lasts much longer, because time is required for the absorption of the blood. Improvement in the swelling in the gums is manifest within forty-eight hours and the swelling is usually all gone inside of a week. Even in cases where there has been a separation of the epiphyses, the epiphyses almost invariably come back into place. It is only in the rarest instances that any permanent deformity of the extremities remains. I have myself seen only one case in which this occurred. In this instance the case had been neglected for a long time and there had been so much ossification of the elevated periosteum that it could not fall back into place.

Treatment.—The first element in treatment is the prevention of the disease. Knowing, as we do, that scurvy develops more frequently in babies that are taking foods made with heated milk or foods prepared without milk, it is always wise to give such babies orange juice or lemon juice to prevent the development of the disease. My experience has taught me that it is necessary to give at least 1 tablespoonful of orange juice daily in order to certainly prevent its development. Hess has suggested the use of potato water, which he has found effective in the prevention of scurvy, in place of the usual cereal diluents, because it is so much cheaper than the fruit juices. He has also suggested the use of the juice of the peel of the orange as an antiscorbutic, as it is both effective and cheap.

When scurvy has developed, it can usually be cured by changing the food. It can almost always be cured by stopping

the heating of the milk, if it is being heated. Recovery is slow when nothing is done but to change the food or to stop the heating of the milk. It is much wiser, therefore, to give an antiscorbutic at the same time, in order that the recovery may be more rapid. Recovery will take place, moreover, when an antiscorbutic is given, even if the food, which was the cause of the scurvy, is continued. The most available antiscorbutic is orange juice. In order to certainly get satisfactory results 2 tablespoonfuls of orange juice should be given daily. Less may not be sufficient; more is unnecessary. It is best to give the orange juice all at one time, one hour before some feeding. It is advisable to give it at this time in order that the stomach may be empty and that the digestion of the milk may not be disturbed. Orange juice may be given plain or diluted with water. There is no objection to sweetening it with a little cane sugar, if it seems desirable. The juice of the orange peel is equally as effective and can be used instead of the juice of the orange. Strange as it may seem, boiling the fruit juices does not destroy their antiscorbutic action.

Boiled and mashed potato also has a definite antiscorbutic action, but potato flour has none. Beef juice has a slightly antiscorbutic action, as have wheat middlings. Their antiscorbutic action is, however, not to be compared with that of the fruit juices and potato. Yeast, cod liver-oil, and olive oil have no antiscorbutic action.

There are no drugs which have any effect whatever in the prevention or cure of infantile scurvy.

CLINIC OF DR. WILLIAM P. GRAVES

FREE HOSPITAL FOR WOMEN

CANCER OF THE UTERINE BODY AS A BORDERLINE CASE IN GYNECOLOGY

HAVING been asked to give a clinical lecture on the subject of borderline cases in gynecology, I am confronted with a certain doubt as to what the expression borderline case really signifies. In fact, I do not for the moment recall having heard it used specifically in gynecologic classification. To my mind the term "borderline case" implies an indecision as to the exact status of a given case in its relation to two specialized branches of medicine, and this condition of doubt may refer to matters either of treatment or of diagnosis, or of both. In my medical school days a borderline case suggested a malady to which the general medical man and the general surgeon both laid claim. In those days the most conspicuous example of such a case was chronic appendicitis. Our eminent professor of clinical medicine was emphatic in his assertion that chronic appendicitis is essentially a medical disease, and should be treated as such, while our surgical instructors, with equal vehemence, held to the view that the chronic appendix should be removed. Viewed from this standpoint cases on the borderline between medicine and surgery are still numerous. If we look for borderline cases in gynecology, we shall find ourselves in a clinical field much too extensive to be treated in detail by a single lecture, inasmuch as cases will be found on a considerable number of different borderlines. For example, one who is interested in orthopedics would be surprised to see in a large gynecologic clinic how many patients apply for treatment on the supposition that they have pelvic disease, whereas, in reality, they are suffering from some bone

or muscle lesion. Again, the boundary lines of gynecology and neurology intersect very frequently, and it is a well-known fact that neurologic clinics abound with patients who need gynecologic treatment, and conversely. In like manner, it will be found that the broad science of gynecology has lines of attachment to practically every specialized branch of medicine, no matter how exclusive, and that at each point of contact there are cases which may properly be designated as "borderline" in the varied significance of the term. As far as general intersest goes, the most practical treatment of my subject would be to discuss those cases that may be said to lie in the borderland of practice between the general practitioner and the gynecologic specialist.

This of itself constitutes a wide range of subjects, but I shall confine myself to a single one which will help to illustrate certain points concerning which there is at present insufficient co-ordination between physician and specialist.

The patient before you is one whom I first saw professionally a little over two years ago. Though seventy-five years of age she was at that time a strong, rugged woman. She had had the menopause at about fifty, but had since then noted an occasional slight show of blood to which she paid little attention. About a year before her visit she had begun to have what she thought was incontinence of urine. She consulted her physician, who made light of the trouble, and without examining the patient prescribed something to allay bladder irritation. The watery discharge continued, however, and as it was rather offensive and was occasionally streaked with blood the suspicion had been aroused in the patient's mind as to whether the discharge really issued from her bladder.

Pelvic examination revealed a large, fixed, tender uterus which bled from the effects of palpation. The cervix appeared and felt entirely normal. There was a watery discharge from the uterine canal, the urine was normal. At the operation it was found that the uterine body was completely invested with a cancerous process which involved both tubes and one ovary. Notwithstanding the extensiveness of the disease throughout

the pelvic organs, *there was no involvement of the regional lymph-glands.*

Please note carefully the points in the pathology of the case, for they are of much significance in the matter of the clinical course of this disease. A complete hysterectomy was performed. The patient made a good recovery and remained in excellent health until about six months ago, or for about a year and a half after the operation.

She comes now for examination for recurring symptoms. Will you examine the patient, Mr. Meigs, and tell us what you find.

MR. MEIGS: I find an indurated area in the posterior wall of the vagina, high up, through which there seems to be some sort of an opening into the rectum. I think there are feces in the vagina. My diagnosis is recurrence of cancer in the vagina, with fecal fistula.

DR. GRAVES: Do you note anything special with regard to the vaginal wall?

MR. MEIGS: It seems unusually tough and leathery, and the whole vagina is curiously shrunken.

DR. GRAVES: Does the presence of a rectovaginal fistula in a comparatively early and well-localized recurrent cancer in the vault of the vagina suggest anything to you?

MR. MEIGS: It seems rather unusual. Perhaps you have been using radium in this case.

DR. GRAVES: You are quite right, Mr. Meigs, radium was given as a prophylactic several times after the operation. The tough shrunken nature of the vagina is characteristic of the result of radiation on normal tissues. The fistula is also undoubtedly the result of a too enthusiastic radium treatment. I have seen a number of postoperative cases like this, in some of which I have applied the radium myself, and in some of which it has been given by others, where fistulas have resulted. This experience has led me to discontinue the practice of using radium as a prophylactic after operation for uterine cancer. I doubt very much if it has any influence in preventing recurrence of the disease, while it causes great risk, even when carefully screened,

of producing vesical or rectal fistulas long after the time of its application, even if the disease does not recur. What is the prognosis in this case?

MR. MEIGS: Absolutely bad, sir.

DR. GRAVES: Could the patient have been saved with an early diagnosis?

MR. MEIGS: Very easily, sir. I have often heard you say that cancer of the body of the uterus is a very benign form of cancer, and that if it is taken anywhere near in time a permanent cure by operation can be practically guaranteed.

DR. GRAVES: Perhaps that is putting my remarks on the subject rather strongly, but nevertheless it is not far from the truth. Now, gentlemen, the history of this patient presents several very important points, which I hope you will remember when you get into general practice and begin to see gynecologic cases.

In the first place, a strong, healthy woman, notwithstanding her advanced age, had noticed for a considerable period of time an occasional very slight showing of blood which was so insignificant that it caused her no alarm. Supposing, Mr. VanStone, that such a patient should consult you, what conditions would you think of, excluding for the moment the possibility of cancer?

MR. VANSTONE: Well, I should think first of a cervical polyp.

DR. GRAVES: That's right, and why?

MR. VANSTONE: Mucous polyps of the cervix are apt to make their appearance after the menopause, and cause intermittent bleeding, quite similar to that of uterine cancer.

DR. GRAVES: Does the presence of a cervical polyp exclude a consideration of cancer of the body of the uterus?

MR. VANSTONE: I should hardly think so.

DR. GRAVES: No, it does not. On the contrary, the presence of a polyp suggests a tendency to activity on the part of the mucous membrane which makes it all the more imperative to investigate the true condition of the uterine canal. What else would you think of in this case?

MR. VANSTONE: Senile atrophy of the vagina will sometimes cause slight bleeding.

DR. GRAVES: That is right.

The epithelium of the mucous membrane of the vagina and vaginal portion of the cervix becomes thin and delicate in old age, and is very susceptible to superficial infections or chemical irritation from abnormal secretions higher up in the genital canal. The vaginal epithelium on account of its thinness readily desquamates under these conditions, leaving small denuded areas that are apt to bleed slightly or to cause a pinkish discharge. The symptoms are exactly like those of an early carcinoma of the uterine body. Now, Mr. Denney, supposing an elderly woman should consult you, complaining of slight hemorrhages from the vagina, and supposing you had examined her and found denuded bleeding patches on the vaginal membrane, would you be satisfied with making a diagnosis of senile vaginitis?

MR. DENNEY: No, sir.

DR. GRAVES: And why?

MR. DENNEY: Because cancer of the body of the uterus appears most commonly after senile atrophy of the genitals sets in, so that a bleeding vaginitis and a cancer of the body might exist at the same time.

DR. GRAVES: Yes, and what is more, the altered secretions from a cancer of the body of the uterus might of themselves set up a senile vaginitis. Here again, as in the case of the cervical polyp, a comparatively innocent lesion which could readily account for the bleeding symptoms should not satisfy the examiner and deter him from taking radical steps for a complete diagnosis.

In addition to cervical polyps and senile vaginitis there are, of course, other non-malignant causes of uterine bleeding after the menopause, such as sloughing fibroids, atrophic atresia of the cervix, myomatous polyps, etc., but these latter are less common and their diagnosis more obvious.

We will now take up the next important point of interest in the case before us. Mr. Thorndike, what symptom or sign of grave significance do you note in this patient's history besides the slight bleeding which we have been discussing?

MR. THORNDIKE: The watery discharge which she and her doctor took to be the result of urinary incontinence.

DR. GRAVES: What can you say as to urinary incontinence occurring suddenly in a healthy woman of seventy-five?

MR. THORNDIKE: I should wish to know whether the incontinence was functional or organic.

DR. GRAVES: Why?

MR. THORNDIKE: Because functional incontinence is usually due to a relaxation of the sphincter muscle of the neck of the bladder. I think it possible that a woman who has borne children might develop incontinence in advancing age. I should think it might also appear as a result of some urethral irritation like that of a caruncle or even from a colon infection of the urinary tract, which I understand is common in elderly people.

DR. GRAVES: As this patient described her symptom to me the watery discharge came away without her knowing it, at any time of day or night, so that she was obliged to wear a napkin continuously. What would you say to that?

MR. THORNDIKE: Under those circumstances the discharge if urinary must have represented an organic incontinence. I mean to say the urine must have escaped through a fistulous opening from the bladder into the vagina or urethra. I don't see how such an opening could suddenly be established in an elderly woman previously healthy. It might, of course, happen in an advanced stage of cancer, especially if radium had been used in her treatment. But there is nothing in this case to indicate that any cancerous process even if present was in more than an early stage when she first sought medical help. I believe there are certain lesions of the central nervous system which produce a complete organic incontinence, but I presume that these may be excluded in this case.

DR. GRAVES: What would be your conclusions?

MR. THORNDIKE: I should conclude that the watery discharge was not urinary at all, but that it probably issued from some disease of the genital tract.

DR. GRAVES: Very good. Then you would not, as this patient's doctor did, tell the patient without examining her that

the symptom of which she complained was incidental to her age and that it need cause no alarm.

MR. THORNDIKE: No, sir.

DR. GRAVES: On the contrary, the appearance of a watery discharge from the vagina should have served as a danger signal of the gravest nature, for it is perhaps more than any other one sign pathognomonic of uterine cancer. It is perhaps somewhat more constantly characteristic of cancer of the cervix than it is of cancer of the body, nevertheless, when it does make its appearance it usually means cancer somewhere in the genital canal. Occasionally a sloughing myomatous polyp will produce the same serous, watery, usually foul-smelling discharge seen in cancer. It always means danger. It represents an exudation of serum through the capillary wall of the numerous new vessels forming in the cancerous growth, and is frequently so profuse, thin, and colorless as to suggest to the patient that there is a leak in her bladder.

This patient whom we are considering did not receive the benefit of a pelvic examination when she first applied for medical assistance. Assume, Mr. Atwood, that she had consulted you when she first noticed the watery discharge, and gave you at the same time the history of having occasionally seen a little show of blood. Assume also that you very properly made a careful pelvic examination and found the vaginal mucous membrane perfectly smooth, the cervix small, atrophic and not indurated, and the uterine body small, movable, and normal in contour. What would have been your conclusions and what advice would you have given the patient? I shall expect you to answer in detail, as you have helped me operate on a number of these cases, so that you may give the rest of the class the fruits of your experience.

MR. ATWOOD: It is possible either for cancer of the cervix or cancer of the body to exist without the possibility of detection either by the palpating finger or by inspection of the vagina through a speculum. Cancer of the cervix nearly always has a suspicious feel to the examining finger, but sometimes the inverting type of growths may become quite far advanced be-

fore being palpable. I should not therefore jump at the conclusion that the patient did not have cancer of the uterus simply because I could not feel it or see it. In order to make more sure of the cervix, I should insert a speculum in the vagina and pass a small curet into the cervical canal. If cancer is present the curet will nearly always bring away a crumbly bit of tissue, with considerable bleeding. If I got a piece of tissue like that I should save it for microscopic examination. If I found no evidence of cervical cancer, I should tell the patient that my office examination was necessarily not complete, and that for final diagnosis it would be necessary for her to have the womb scraped under an anesthetic in order to make a microscopic examination of the lining membrane of the womb. If the patient objected or wished to put it off until some later date, I should urge the necessity of operation.

Dr. Graves: And if she still persisted in her objections I should deliberately tell her I wished to find out definitely whether or not she had a *cancer*. The use of that word will always bring the patient to her senses. Go on, Mr. Atwood.

Mr. Atwood: The next step would be to take the patient to a hospital, and, under ether, to curet the uterus, for the purpose of examining the curetings by microscope.

Dr. Graves: Yes, and it is important to save the curetings for examination even if they are very small and do not suggest cancer by their gross appearance. A beginning cancer of the body in an atrophied mucous membrane may make a very insignificant showing in the curetings.

We will now return to the case under consideration, and you will recall that as a result of neglect the disease was found at operation to be very advanced and to have involved the uterine wall, the tubes, and the ovaries, but that there was no involvement of the regional lymph-glands. The local pathology of this case is very instructive in that it illustrates well the typical course that cancer of the uterine body takes. It always has its origin, as you know, in the endometrium, that is to say, in that part of the uterine mucous membrane which is above the internal os. At first the disease is localized, forming a wart-like ex-

cresence projecting into the uterine canal. The little papillary filaments of which the small growth is composed break off easily and cause a slight show of blood. This is a fortunate circumstance, for it gives the patient a warning signal early in the disease. The warning is especially apt to be heeded by the patient since cancer of the uterine body is more common after the menopause when the appearance of abnormal bleeding is more likely to cause apprehension. In this respect, as in every other, cancer of the fundus is less treacherous than cancer of the cervix, which may progress to a hopeless stage without a sign or symptom to indicate its presence.

Cancer of the body of the uterus progresses rather slowly. The disease spreads out over the mucous membrane and dips down into the muscular wall of the uterus. It has very little tendency to metastasize. Curiously enough, metastases when they do occur appear first in the ovaries, and this is a fortunate circumstance, for it tends to confine the disease to a tissue area which can easily be eradicated by operation.

Involvement of the tubes is by direct extension late in the disease. Invasion of the parametrium and of the cervix takes place only in very advanced stages.

Thus you will see, gentlemen, that cancer of the body of the uterus is from the standpoint of surgery a very favorable disease, in that it gives early warning, grows slowly, metastasizes late, and occurs in a group of organs which are easily removed. The percentage of permanent operative cures is very high, higher probably than in any other form of deep cancer. And yet it is extraordinary how many women who have this entirely curable disease will allow themselves, or be allowed by their physicians, to drift into a stage of inoperability.

Cancer of the body of the uterus, although most commonly a disease of the postclimacterium, is by no means confined to that period of life. It is frequently seen in the forties, and occasionally, though rarely, before. It is also often associated with fibroids, especially with those tumors that have attained a considerable size. The clinical diagnosis of cancer of the uterine body before or during the climacteric is less simple than

after the menses have ceased, as its symptoms are easily confounded with those of several other diseases which are apt to make their appearance in the fifth decade. A full discussion of cancer of the body at that period would entail a review of the whole subject of the menorrhagias and metrorrhagias of the menopause, which is one of the most important in gynecology, and one to which we have time in this lecture to make only a brief reference.

Cancer of the uterine body occurring near the menopause may, according to our special definition of the term, be justly classified with borderline cases for the reason that the abnormal bleeding that it causes is so frequently regarded by the general practitioner as a physiologic incident of the change of life, and therefore treated medically.

One reason why the diagnosis of cancer of the body at this period is so frequently missed by the physician is that it may give no palpable evidence of its presence in the uterus until the disease is considerably advanced. Cancer of the cervix usually causes at an early stage a suspicious hardness of the cervical lips which those physicians who take the trouble to examine their patients are, I am glad to say, learning to detect with increasing accuracy. Fibroids of the uterus are usually easy of diagnosis, especially as many of them can be readily palpated through the abdominal wall. In cancer of the body, however, the cervix is normal, and the size, consistency, and contour of the fundus may for a considerable time suggest no anatomic abnormality. In the absence of complicating fibroids, the clinical course, and findings from pelvic examination may exactly simulate those associated with the comparatively harmless condition of uterine insufficiency, which, as you know, is an extremely common affection of the menopause period. As most cases of uterine insufficiency will if the patient waits long enough become cured spontaneously, an erroneous impression has been created among the laity and among some of the profession that abnormally profuse bleeding is a physiologic phase of the menopause. This is a dangerous doctrine and has led to the death of many hundreds of women whose lives might have been saved by timely surgical interference.

I cannot be too emphatic in impressing on you that the normal menopause takes place by a sudden or gradual cessation of the menstrual flow. If at the climacteric age the flow is increased in quantity or in frequency or by a prolongation of the menstrual period, or by intermenstrual hemorrhages, the change must be regarded as abnormal, and immediate steps must be taken to insure an accurate diagnosis. In the absence of some obvious lesion, this can *only* be done by an examination under an anesthetic, with a removal by the curet of sufficient endometrium for microscopic section.

If this rule is rigidly carried out with every case of abnormal menopause bleeding it will be found that the majority of cases without palpable cause for bleeding will turn out to be uterine insufficiency. Nevertheless the number of cases of cancer in the whole number examined will be surprisingly large.

Subjecting a patient to the annoyance of a hospital ether examination and finding only a uterine insufficiency is not a matter to be in any way deplored. The ability to tell a woman who has been bleeding that she positively has no cancer not only gives immense mental comfort to the patient, but relieves the attending physician of a grave responsibility.

Moreover, uterine insufficiency, whether it be from a functional ovarian disturbance or from chronic tissue changes in the endometrium, is itself a disease which may have very serious effects on the patient's general constitution and especially on her nervous organization. If at the time of excluding the presence of cancer the abnormal bleeding may also be checked or the menstrual function completely stopped according as circumstances demand, the operation is still more desirable. Fortunately, we have in radium an almost specific cure for the hemorrhages of uterine insufficiency, and though at the present time it is available only in the larger medical centers, it will not be long before hospitals everywhere will be equipped with sufficient quantities for the treatment of this common and depleting affection.

In concluding the lecture I may sum up the points that I wish you to remember as follows:

1. Cancer of the body of the uterus may be classed as a borderline case because of the frequency with which it is treated medically by the general practitioner.

2. The slightest show of blood after the menopause should demand an immediate curetment of the uterus for microscopic diagnosis of the endometrium even if the bimanual examination reveals nothing abnormal to the touch.

3. Cancer of the uterus, both of the fundus and cervix, often causes a watery discharge which simulates urine. A watery discharge from the vagina is, therefore, a signal of danger.

4. Cancer of the uterine body grows slowly and is operable long after its initial symptoms.

5. Cancer of the uterine body is the most favorable for operation of all deep cancers because of its slow growth, late metastasis, and long confinement to a group of organs that can easily be removed.

6. Cancer of the uterine body may occur in the menopause decade, and simulates in its symptoms especially uterine insufficiency.

7. The menopause is normally characterized by a lessened flow of blood. Increase of blood at that time is an important danger signal.

8. Increased flow near the menopause should always be investigated by microscopic examination of the cureted endometrium, even if digital examination reveals no anatomic abnormality.

CLINIC OF DR. CHARLES J. WHITE

HARVARD MEDICAL SCHOOL

SOME COMMON ERRORS IN DERMATOLOGIC DIAGNOSIS AND TREATMENT

Errors of Omission and Commission in the Diagnosis and Treatment of the Commoner Diseases of the Skin. References to Certain Methods of Treatment which Do Not Figure in the Text-books.

As the years pass in my public and private consultation practice I am struck more and more by certain definite errors of omission and commission on the part of the general practitioner in his diagnosis and treatment of certain skin diseases. No great blame should be attached to such errors, for nowadays no one man who may be called upon to treat every conceivable human ailment can possibly know all that is known by those who give their entire time to one division of medical knowledge. What follows, therefore, is not to be taken as a personal criticism by any member of this audience, but should be received in the spirit in which it is given, *i. e.*, the crystallization of the thoughts of one who has witnessed these errors and seeks a method of preventing their future recurrence. What follows, then, will be a résumé of the commoner errors in diagnosis and references to certain methods of treatment which may not figure conspicuously in the text-books, but have proved of distinct worth in my hands.

ERYTHEMA MULTIFORME

There are individuals who are bothered with frequent recurrences of this disfiguring and often incapacitating disease which previous treatment has not cured. In such cases let me

advise you to try one or the other of the following methods internally, and remember that the drugs should be administered not only through the immediate attack but also for several months, even five or six, afterward, with one week's intermission out of every four. The first drug is hexamethylenamin in 5-grain doses after each meal in a full glass of hot water. If this fails after a thorough trial, then substitute calcium lactate to the amount of 10 grains in a half-glass of warm water after meals. To gain the full benefit of this latter drug under all circumstances the patient should eschew all acid foods, *i. e.*, raw fruits in any form, all types of pickles, tomato, cucumber, and vinegar, and should make a point of eating the lime-rich foods, such as milk, eggs, and spinach. Externally "white wash,"

℞. Acid. carbol..... 2
Calamin..... 4
Zinc. oxid..... 8
Aq. calcis.....q. s. ad. 250

always gives rapid relief to the burning and itching, and quickly dries up the ever-present edematous lesions. This wash should be sopped on (never bandaged) every hour until the lesions are stiff and dry, and when the skin seems about to crack from stiffness "Lassar's paste,"

℞. Acid. salicyl..... 0.65
Zinc. oxid..... 2
Amyl. maidis, vaselin.....āā 15

should be applied night and morning under one layer of old cotton or linen.

URTICARIA

The simple attack of "hives" following, in susceptible persons, the ingestion of certain well-recognized foods is usually easily relieved by a good saline purge, moderate fasting for a few days, and the application of any of the common antipruritics. There is, however, a decided proportion of these "sensitized" individuals who find their way, sooner or later, in despera-

tion to the dermatologist because endless previous medication has not relieved them from their intolerable itching and its resulting insomnia. These patients are usually women, and practically always of the "nervous," high-strung type, probably with a superfunctioning thyroid at the bottom of their troubles.

First of all, if possible, one must take these patients out of their present environment and occupations; rest should be the foundation of their cure. It is an accepted fact that a change of scene, of people, of food, of family surroundings is perhaps our best "tonic." If possible, arrange for such a change. For a few days starve these people on a diet of bread, butter, rice, and water; and then cautiously add simple roasted or broiled chicken or beef, baked or boiled potato, or macaroni, string beans, peas or spinach, and simple farinaceous puddings plus milk or freshly brewed tea. Great stress should be laid on the avoidance of all acid foods (see under Erythema Multiforme) and of coffee. Calcium lactate again is our standby internally. Every night, just before going to bed, these patients should take a starch or a soda bath. This means a warm bathroom; a pound of cornstarch or of cooking soda to the tub of water; temperature of water 95° F.; quiet immersion without soap for five minutes; drying by patting and not rubbing with a soft Turkish towel. Neither silk nor wool should be worn next the skin. Before the patient enters the bed some one should warm the sheets by passing a hot-water bottle between them. Cold and heat bring on paroxysms of wheals, and scratching and both extremes of temperature should be avoided. Externally an ointment of menthol,

℞. Menthol 1
Zinc. oxid. 2
Vaselin 30

seems to be the most successful application.

If these combined methods fail, we can have recourse to the *x*-rays in analgesic doses, but this maneuver must never be undertaken by anybody but an expert. Such a combination of procedures practically never fails if co-operation has been sincere.

It may be necessary, however, in certain extreme cases to resort to skin tests to determine what is the noxious element present. Let me illustrate this point. Recently a young man was unsuccessfully treated according to the above methods, except that *x*-ray exposures were impossible because of his distant domicile in a small town. It was noted that his worst recurrences invariably followed an evening at the theater or the movies. Skin tests showed an intense susceptibility to rice, and it was evident that the exposure came through inhalation of rice powder from the skins of his "fair" neighbors in the hot, ill-ventilated auditoriums he frequented.

DERMATITIS EXFOLIATIVA

When confronted with this essentially scaling disease it is only natural for the practitioner to combat this condition in the customary way, that is, by the application of ointments. Dermatitis exfoliativa is a serious disease, and up to a certain date the skin records of the Massachusetts General Hospital showed that 50 per cent. of its patients afflicted with this disease had died under treatment. Then we began the so-called "dry treatment," and from that moment until the present day it is a fact that no patient with dermatitis exfoliativa, who has been treated *completely* by this method, has been lost. Nevertheless, the convalescence is commonly desperately tedious, the cure running into months.

The "dry method" consists in the superabundant application of borated talcum powder and imperatively nothing else. The patient should be placed in a room devoid of all carpets, rugs, hangings, pictures, and furniture—nothing save the bed is left. The hair should be cut close and the powder should be dusted on whenever in the twenty-four hours a single fraction of an inch of skin becomes visible. The patient should, in fact, lie in a bath of powder. Loose plugs of absorbent cotton should be placed in each nostril and there should be demulcent drinks for the dry throat and 10 per cent. argyrol solution for the eyes, because at times the facial orifices become painfully irritated by

the particles of powder floating in the atmosphere. All bathing is indefinitely suspended.

The first week or two of this intensive dry treatment may be, and usually is, a period of agony, for great cracks and crevices develop here and there over the body, and the patient and his family beg and plead for "just a little ointment" to soften the overlying crusts formed by the resultant oozing of serum. The physician must be as hard as adamant against these pleadings. This phase must be gone through with, and the sooner it is over, the better for all concerned, for afterward it never recurs, granting that there has been no digression, even by a hair's breadth, from the hard-and-fast line of the "dry treatment." If pus forms under the crusts, they must be forcibly lifted or cut away and more powder applied. It may be proper here to apply for fifteen minutes night and morning "black wash":

℞. Hydrarg. chlorid. mit. 2
Aq. calcis. 250

The comfort of the patient can at all times be enhanced by the use of an air-mattress and cradles to keep the clothes from the tender skin. Sterilization of all bed and body linen is obligatory, and a constant and steady supply should be on hand. The patient should be given an easily digested, light, but supportive diet, and possible intercurrent symptoms should be treated at once. There should always be plenty of fresh air, day and night, and suitable and cheerful companionship, if possible, should be provided. Let me repeat that the cure is discouragingly long drawn out; more than once we are tempted to try some other method, but let us always bear in mind that death has, as yet, never claimed any patient of ours who has been treated absolutely conscientiously by this method.

LICHEN PLANUS

The unwary physician has often been trapped into serious errors by this disease, either through ignorance or carelessness. The chief pitfall is the differential diagnosis between this disease and syphilis.

A papular syphilis may itch, and, in course of time, by the friction of scratching or of the clothes and by the natural subsidence of the lesions, the tops of the papules may become flat and glistening, and the sides may lose their original rotundity and the color may become tinged with blue, and then we are confronted, to a greater or lesser extent, with the subjective and objective symptoms of lichen planus. Let us all, however, remember the existence of this disease, and then with our modern means of diagnosis we can practically always prove the existence or the absence of dreaded syphilis.

There is, however, a form of lichen planus which can trap even the expert unless he be "on his toes," or unless he be a thorough routinist and has submitted his patient to the "dark-field" lens and the Wassermann test. This variety is known as lichen planus annularis, and curiously enough it has a decided predilection for the glans penis or its shaft or the scrotum or the lower abdomen. Lichen planus annularis and an annular syphilid require diligent circumspection and diagnostic acumen to differentiate between. History and modern laboratory tests will, of course, settle the question, but let us not forget the possibility of such a delicate clinical confrontation.

LICHEN SIMPLEX CHRONICUS (LICHEN CIRCUMSCRIPTUS)

These terms signify a definitely circumscribed, thickly infiltrated, dark red, minutely scaling, painfully itchy plaque somewhere on the trunk or the extremities, or at the base of the skull of a "nervous" individual—usually a woman and one approaching or in middle age. Endless drugs in various forms have been advocated and applied in this dermatosis, but despite these many previous failures, two methods of treatment have proved themselves trustworthy and successful.

If the attending physician is a man experienced in the cutaneous therapeutic use of *x*-rays he can soon bring about the relief so ardently desired by the long-suffering patient. If the physician cannot honestly qualify as such an expert, he should immediately send his patient to one who can. If this sacrifice on the physician's part is not possible, and very often, through

lack of time or money on the patient's part, or through distance, the transfer is not possible, then let him have recourse to crude coal-tar, and very likely the desired cure may be just as successfully and rapidly attained.

Crude coal-tar is one of the first products of the burning of bituminous coal—a black, tarry-smelling, viscous semisolid or liquid. One can now obtain it through the Eastern Drug Company. This substance, first introduced into dermatologic practice by Brocq, of Paris, has proved one of the great therapeutic "finds" of recent years. For use in the hair it should be combined with vaselin and applied between the hairs by means of a fine swab; for use on a dry surface it should be mixed with lanolin; and for applications to a moist condition it should be incorporated in a paste. It should perhaps be tried first in a 5 per cent. strength, and should preferably be diluted with an equal amount of zinc oxid. It is, unfortunately, a dirty, esthetically unacceptable medicament, and it smells; but its wonderfully successful therapeutic properties far outweigh its outward disadvantages. It naturally stains linen badly, but thorough rubbing with lard and subsequent washing in hot water and soap will usually remove all traces of discoloration. Before each morning and evening cutaneous application the old remaining portions should be removed with oil of sweet almonds—water should never be applied. During the use of crude coal-tar positively no other drugs should ever be employed locally; all hair at the site of applications should be kept closely cut; if pustules appear the inunctions should cease and not be resumed until all pus has disappeared; and there should be no bandaging over the affected area. Long experience has taught the necessity of these hard-and-fast rules.

PSORIASIS

From a diagnostic point of view we should not forget that in the macular, delicately scaling types of psoriasis the disease may closely resemble eczema psoriasiforme and pityriasis rosea; and that in its later, infiltrated, serpiginous, and at times moister stages psoriasis is quite easily confounded with syphilis and with

lupus vulgaris. Such possible mistakes naturally entail serious therapeutic and prognostic blunders.

Concerning the treatment of this at times almost hopelessly intractable disease let me make two suggestions: There is a multiple, highly inflammatory type of eruption where all of the usual, exciting, detergent drugs serve only to add fuel to the flames. Here we can apply a mild ointment and frequently derive rapid and gratifying benefit:

℞.	Bismuth. subnitrat.	2
	Acid. boracic.	4
	Ol. olivarum.	8
	Lanolin	24

More frequently we are confronted with old, desperately chronic, deeply infiltrated, thickly desquamative plaques which cover large areas of the trunk and limbs. Preceding medical attendants have tried numberless medicaments. In such cases we at the Massachusetts General Hospital, at the instigation of Dr. Loretta Joy Cummins, have instituted the carbohydrate-poor diet, applying to the surface only the most perfunctory medication. We still have our failures in these trying cases, but we feel assured that their numbers have been decidedly diminished since we have perfected this method.

This radical procedure is not advisable in growing children, on account of the possibilities of an ensuing acidosis and because we consider the natural growth of the child more important than the incidence of psoriasis. We do not advocate this selective starvation for the thin type of adult. Therefore, bearing in mind the possibilities of acidosis and of too great loss of weight, we begin the treatment. We give each patient printed sheets of the Allen diabetic diet and recipes for the making of bran and agar cakes and bran and Lyster flour muffins and doughnuts. We insist on accurate weight charts from each patient and we stop the diet if it is found too depleting. In the first week there is always a loss of 3 to 4 pounds, and in the succeeding three or four weeks a further weekly loss of perhaps 2 pounds more. Then equilibrium is apt to be established and from then on there is usually no further loss.

This little-known method may seem decidedly bewildering, for previous dietetic investigators have strongly urged the elimination of protein from the daily bill of fare. My only answer is, try for yourself this more recently advocated method. My only explanation of these contrary teachings is that, after all, perhaps the value of either lies in the semistarvation of the patient.

PITYRIASIS ROSEA

Diagnostically, let me emphasize two very frequent errors. The first is the mistaking of this disease in its early, undifferentiated, macular stage, for syphilis—naturally a very serious blunder, but, unfortunately, in my experience, not at all a rare one. The second, even more common, is the confounding of this disease with multiple tinea circinata. The fault generally lies in forgetting that there is such a malady as pityriasis rosea. Bearing constantly in mind the existence of this harmless affection will easily obviate these unfortunate errors, and the use of the microscope and the Wassermann test will render the proper diagnosis a comparatively easy matter.

Therapeutically let me warn against the use of strong applications in this affection; they are not only unnecessary but also distinctly harmful. It is not an exaggeration for me to state that in my experience the great majority of patients with pityriasis rosea have been overtreated by their first attendants, and come to me with lesions so inflamed that the proper diagnosis is often a matter of great difficulty. Generally, the first physician has considered the outbreak to be ringworm, and has prescribed tincture of iodin, mercury in some form, or sulphur, and the result is a weeping or semimoist dermatitis venenata. Whatever our beliefs may be concerning the etiology of the disease, the fact remains that pityriasis rosea is best treated by means of soothing applications; and in my own hands "white wash" (*vide* Erythema Multiforme) in summer and "pink wash"

℞.	Acid. carbol.	1.30
	Calamin.	4
	Zinc. oxid.	8
	Glycerin.	8
	Aq. destillat.	q. s. ad. 250

in winter have proved entirely satisfactory from a curative and from an esthetic point of view. Winter, in the climate of Boston, means the period from September 15th, to June 1st; summer, from June 1st to September 15th. These washes should be sopped on whenever and wherever subjective symptoms arise; the diet should be "light"; the clothing should be non-irritating and loose; work, especially in warm weather, should be kept down to a minimum; and a starch bath (*vide* Urticaria) should be taken, if acceptable, once a day.

ECZEMA

The diagnosis of this common disease is usually comparatively simple, save in the palms and soles, and in these areas the general practitioner must be on his guard lest he confuse this disease with syphilis, or with psoriasis, or with infection by the Epidermophyton inguinale, a relatively unrecognized variety of the ringworm plant. Syphilis and psoriasis of the palms are adequately described in the text-books and should require no reiteration here, but the clinical appearances of Epidermophyton inguinale infection have not been as yet sufficiently elucidated except in the very latest editions of dermatologic treatises, and may very properly be detailed at this juncture.

Most of us are acquainted with this plant in connection with the sharply demarcated, pink-red, delicately scaling homogeneous plaques found on the inner upper thighs, next the pubic arch and, usually on the left side in men, because of the contiguity of the scrotum. We have called this "red flap," eczema marginatum, jockey-strap itch, etc., but now, thanks to Sabouraud, of Paris, we know this to be due to a certain type of ringworm. More recently we have learned that similar conditions may arise over the pubes, around the umbilicus, in the axillæ, along the perineum, between the nates, and in the bend of the knees and elbows. Let us, therefore, not forget these pitfalls, for we may treat these infections as eczema for an indefinite period and get no results; whereas a proper diagnosis plus the application of Whitfield's (of London) ointment will ensure a cure in these areas in a comparatively few days:

℞. Acid. salicyl..... 2
Acid. benzoic..... 4
Adipis benzoat..... 30

Within the last two years we have learned that this same plant, the Epidermophyton inguinale, may produce lesions on the palms and soles, between the fingers and toes, and, to a lesser extent, on the contiguous dorsal surfaces of the hands and feet. To simplify the description of these relatively unrecognized infections let us divide them into the dry and the moist types.

Dry Type.—Between the toes, for instance, we may be confronted with stratified scaling, which, at the bottom of the space, where heat and moisture are the greatest, may take on the consistency and color of lard. This condition is apt to be most prevalent (for the reasons just given) between the fourth and fifth toes. Questioning will reveal the fact that this desquamative condition has probably persisted for months and even for years, and that in most cases, for obvious reasons, it is most conspicuous in the warmer months of the year, often in winter dying down into almost nothing. From these one or more foci we may note a delicate redness and roughness and desquamation extending outward and backward, always with a fairly well-defined circular border, on to the plantar surface of the foot or more rarely on to the dorsal face. The exact prototype of this clinical picture may and does occur between the fingers (but always, naturally, to a lesser extent) and on the palms and backs of the hands, where the condition may be more extensive and more intense than on the feet. Itching is usually present and may be violent.

Moist Type.—Here we are dealing more with the lateral aspects of the fingers, the middle of the palms and of the soles, and especially with the arch of the foot. The horny layer in these parts (except that of the digital sites) is decidedly thick, and we note first a deep, seemingly intracutaneous vesicle which sooner or later becomes semipurulent, reaches the surface, breaks, and often forms a minute opening surrounded by a curious, collar-like scale. These primary vesicles are apt to

form in groups, and the resulting phase produces a strikingly cribriform area with diminutive serpiginous outlines. In earlier years we have called this condition dysidrosis and dermatitis infectiosa eczematoides, and possibly dermatitis repens. It is not my intention to claim that these diseases do not exist, but it is my present purpose to emphasize the fact that the Epidermophyton inguinale can be demonstrated in numerous examples of these hitherto frequently improperly diagnosticated skin eruptions.

When once the correct diagnosis has been made it is a pleasure to both patient and physician to observe the rapid subjective and objective relief from what has, up to this moment, proved an intractable and perhaps even cripplying condition. This rapid change is produced by the inunction of Whitfield's ointment (*vide supra*), by the daily washing of the affected parts, and by the sterilization of gloves and stockings.

From a therapeutic point of view of eczema I want to speak of two types—the infantile and the winter varieties—of the disease.

Eczema generally attacks babies in one of two ways. As a rule, the moist form predominates and consists of redness, edema, excoriations and crusts on the face and forehead, and, to a lesser extent, on the scalp, buttocks, hands, and flexures. Relatively occasionally we meet the dry, slightly infiltrated, somewhat scaly type of the disease. In the latter case the eruption is liable to be on any portion of the body.

The introduction of crude coal-tar (*vide* Lichen Simplex) has, in my own experience at least, revolutionized the treatment of infantile eczema of the wet type. Before its introduction one could count on two winters and an intervening summer of treatment. One was obliged to insist on the use of masks and the constant fastening of the victim's hands to the bed. The mother or attendant nurse required an extra pair of hands with each change of the child's dressings to prevent severe damage to the uncovered skin—more damage than could be repaired during the succeeding interval of treatment; and despite all these cares and anxieties the child remained in the greatest

discomfort and the disease failed to disappear. Now the picture has changed. The constant exhibition of crude coal-tar, employed in the proper manner, within a few hours usually controls the itching, and within a comparatively few days cures the disease in the majority of cases. There must, of necessity, be exceptions to this rule. Then we insist on a microscopic examination of the patient's feces, which in these wet cases usually reveals the child's inability to digest its fats. We then naturally reduce the ingestion of fat or of starch, if that be the case, and proceed with the crude coal-tar as before. Even then a few recalcitrant examples persist, and in such an event we make cutaneous food tests, when finally we may discover the noxious etiologic agent. Unfortunately, the dry cases of infantile eczema hold out no such rosy outlook. Here crude coal-tar is utterly unsuitable and no genius has found its counterpart.

The treatment of winter eczema is not difficult when one bears in mind the fact that the redness and the delicate scaling and the itching are due to the dryness of the atmosphere, which begins in the latitude of Boston about September 15th, and continues well into the spring. Apart from the dryness of the atmosphere we live frequently in houses heated by hot-air furnaces, we take hot baths, we use drying soaps, and many of us, both men and women, no longer wear long-sleeved and long-legged underclothes.

To counteract these ill-effects let us lay down certain definite rules for every-day life, and let us warn our patients to begin to observe these instructions early in the autumn when dog-days have left us and the cool, invigorating northwest winds begin to blow. Have pans of water on every radiator and keep the furnace water-boxes full. Cultivate as many growing plants in the living rooms as possible. A starch bath (*vide* Urticaria) should be taken every night, using a superfatted cold-cream soap. Wear tight-fitting sleeves to the shirts and long legs to the drawers. Wear no silk or wool next to the skin, but, if wool is necessary, let it be worn outside of cotton. Before dressing in the morning, after undressing at night, and whenever the skin itches or tingles or burns apply warmed "pink wash" (*vide*

Pityriasis Rosea). If there is an appreciable amount of infiltration and scaling, a distinctly greasy, mild ointment is very grateful:

℞. Bismuth. subnitrat..... 2
Ol. olivarum..... 8
Lanolin..... 24

Severely intractable cases of winter eczema, especially in old people, are not always cured by these methods, but analgesic doses of *x*-rays from an expert's hands practically never fail to relieve and to cure this troublesome condition.

HERPES SIMPLEX

Many a golden opportunity has been lost in confusing "cold sores" and the initial stages of hard and soft chancres. There is only one maxim to follow: When in doubt, take a smear and examine it under the dark-field lens or stain this smear and study it under the oil-immersion lens. Ignorance or carelessness in differentiating these frequently confronting clinical similarities are grave offenses against a patient's rights.

One is often consulted by individuals who suffer from recurrent attacks of herpes on the lips or the cheek or the genitals. In such cases the long-continued ingestion of hexamethylenamin has not infrequently eventually stopped this annoying condition—5-grain tablets dissolved in a whole glass of hot water and taken after each meal for perhaps two months, and then less and less frequently for many weeks, have proved efficacious in my hands in more than one instance.

HERPES ZOSTER

A word of caution here as to the diagnosis of this disease. Quite often a neuralgic stage may precede by some days the actual cutaneous eruption. Patients have been treated by physicians merely for their nerve disturbances, and no cutaneous examination has been made. One rather remarkable instance recurs to my mind. A lady consulted an aurist for pain about the right ear; in a few days she consulted an oculist for a similar

condition of the right eye; then she asked the assistance of a medical man because of a right-sided headache; then she went to a surgeon because of pain in the right side of her neck. The surgeon asked my opinion, and inspection revealed a few groups of rather abortive vesicles scattered through the thick hair on the right side of the head. This, of course, is an extreme case; but not at all rarely does one find an obscure, antecedent neuralgia, the nature of which is eventually divulged by the subsequent characteristic eruption of grouped vesicles.

Don't let us forget that freezing the seat of the affected nerves twice daily with ethyl chlorid will cause rapid relief from the painful accompanying neuralgia, and will, in all probability, ward off the frequent and long-continued neuralgic after-pains which are especially severe in elderly people.

POMPHOLIX (DYSIDROSIS)

Whenever confronted with these closely allied conditions be sure to rule out the possibility of an Epidermophyton inguinale infection. Plant some of the fluid on Sabouraud's medium,

℞.	Peptone	0.50
	Agar	1.30
	Maltose	3.80
	Water	100

or examine the fluid under a high-power lens, excluding much of the light. Let me warn you, however, that the presence of this hyphomycete is never easy to demonstrate.

IMPETIGO CONTAGIOSA

The general practitioner recognizes this disease in most instances, but there are two varieties of the infection which are very apt to lead one astray. Occasionally in the newborn we meet with an abundant bullous eruption about the nates, and less often around the genitalia. In my experience this condition is practically always called syphilis, sometimes pemphigus, almost never impetigo contagiosa. Nevertheless it usually is impetigo contagiosa and strict asepsis plus an ointment of

℞. Acid. salicyl..... 1
Sulph. præcip..... 1.5
Adipis benzoat..... 30

will usually cure these really sick babies. The second confusing type of the disease, and one which seems rarely to be diagnosticated properly, is the circinate form where one notes large round circles of crusting moisture, sometimes in concentric forms. This is a rare variety, but it yields equally well to antisepsis and the application of a suitable ointment.

As to the treatment of the disease in general, my criticism would be that the presence of pediculi capitis has not been duly considered; that sufficient stress has not been laid on antisepsis (the key to the whole success of its management); that the barber has been allowed to continue his various ministrations without proper instructions; and that too strong applications have been employed. Gentle shampoos with powdered soap; drying with fresh, sterilized gauze; freshly boiled pillow-cases and sheets and handkerchiefs every day; repeated washings of the hands; the use of fresh gauze instead of shaving brushes, and of powdered soap and of boiled razor-blades in shaving; and the constant use of one of the following ointments will invariably prove successful within a week or ten days:

℞. Acid. salicyl..... 2
Sulph. præcip..... 2
Adipis benzoat..... 30

or

℞. Hydrarg. chlorid. ammoniat..... 0.13
Acid. salicyl..... 2
Adipis benzoat..... 30

DERMATITIS VENENATA

This important disease seems to provoke the greatest number of pitfalls for the unwary practitioner both in diagnosis and in treatment. To be a master of this common, trying, and not infrequently crippling condition one should have the detective powers of a Sherlock Holmes and the most intimate knowledge of the world's irritants, whether of the animal, vegetable, or

mineral kingdoms, whether used or encountered in work or at play or in mere existence.

It would be impossible here even to enumerate the world's noxious substances or the various trades, occupations, pastimes, and practices which expose one to them; suffice it to say that they are endless, but that, fortunately, most of us are immune to their influence. Nevertheless, the victims are many, and it should at least be our duty to recognize them at the very first opportunity and to treat them properly. I regret to say that we who practice medicine are not all experts in this special branch of medical knowledge—far from it in fact. In the first place, don't call this disease erysipelas, and second, try to master the special features which separate this affection from eczema. The differences are very subtle at times and perhaps impossible wholly to put on paper. However, when you observe a rather indefinite, possibly blotchy redness, and particularly even a tendency toward vesiculation, especially when these lesions are accompanied by itching and occur on exposed places, always suspect some external irritant, and begin at once to ply your patient in the most inquisitive manner concerning his occupation, his habits, his customs, and his pleasures. Bear in mind especially the possibility of poisoning by furs, hair dyes, poison ivy, and the poisonous primrose.

In regard to furs, remember that it is toward spring when the neck perspires that the dye is most apt to be dissolved. Therefore don't be led astray by the remark that "it can't be this (coat or this boa), because I have worn it all winter." Be on the lookout for lusterless hair and don't be afraid to ask questions, although one must use tact in dealing with this type of patient, for people who dye their hair are apt to be "touchy." Remember that the smoke from bonfires containing the wood of poison ivy is particularly potent, so don't exclude this type of poisoning even in winter. Finally, don't forget the existence of the poisonous primrose, usually the Primula obconica, for in winter this plant plays a large rôle in the production of dermatitis venenata. I shall always remember one consultation. I was called to a neighboring town to treat a case of "recurrent

erysipelas." On entering the patient's room I found her sitting beside a table covered with these insidious plants. The "recurrent erysipelas" was easily cured. It used to be an easy matter to identify this plant, for in its original guise it consisted of a relatively large olive green leaf the shape of the ace of spades, and covered on its under side with many whitish hairy spines; of a long stem covered with spines similar to those on the leaf; and of a cluster of ten or twelve small, delicate, pale lavender flowers. Nowadays this description holds true only of the hairy spines, for through the manipulations of the florists the leaf is of a lighter color, the stems are not so long, and the flowers are considerably larger, and may be pink or red.

Let us consider dermatitis venenata from the point of view of location. If the ears and forehead and scalp are affected, think of hair dyes or the possible application of kerosene. If the neck and upper chest are involved, ask about furs, and remember that the suspicious ones are usually those which lack luster and are dead brownish or dead blackish in color. If the trouble lies in the axillæ and their neighborhood, inquire into the question of depilatories and preparations against perspiration. If the pubes and the penis are inflamed, look for pediculi pubis, and query the patient about the use of kerosene and especially "blue butter." If the penis and scrotum are red and edematous, suspect poison ivy. When the disease affects the face and hands no immediate inference can be drawn, because these necessarily exposed surfaces may come in contact with almost any conceivable irritant, according to the special circumstance.

The treatment of dermatitis venenata should be a very simple question, and if the cause can be determined the cure should be possible within a week or two, granted, naturally, that the proper measures are advised by the physician and strictly followed by the patient. Past experience, however, has demonstrated very clearly that treatment in very many cases has not been so successful as it should be.

The importance of this subject and the possibility of easy and prompt success warrant a thorough exposition of at least

one efficacious method of treatment. It is assumed, of course, that the cause of the dermatitis has been thoroughly investigated and determined if possible. The patient is first advised to take a bath, which should include the scalp, face and hands, and whole body, using plenty of soap and rubbing down afterward with alcohol. This precaution will probably do no harm, and may prove very successful in aborting subsequent development of the disease in other parts of the body. The patient is then advised to stop work and to stay at home in loose garments; to live on the lightest and most digestible diet; to take a diuretic,

℞. Potass. acetat..... 32
Aquæ..... 250
Sig.—A tablespoonful in a whole glass of water t. i. d., p. c.

to keep the bowels freely open; to sop on "white wash" (*vide* Erythema Multiforme) every hour (avoid all bandages) until the skin looks and feels like a whitewashed fence; and to drop into the eyes, if the lids are closed, a 10 per cent. solution of argyrol.

This stage of the treatment should not require more than a week, possibly not more than two or three days. When the skin is stiff and hard and even cracked, and is oozing serum, then begin the second stage of the treatment—the process of repair. Apply "pink wash" (*vide* Winter Eczema) twice a day, and as soon as it has dried smear on Lassar's paste (*vide* Erythema Multiforme). This should be covered with one layer of thin old cotton or linen cloth fastened by safety-pins. This second phase of the treatment usually requires only a week or somewhat more. Contrast this rather seemingly rosy prognosis with the possibilities of maltreatment. From a rather long consultant experience, in which more than a few instances of unsuccessful treatment of dermatitis venenata have been encountered, two especially striking cases recur to my mind. A man said that he had been poisoned by ivy two weeks previously, and presented what looked like an extraordinarily large arm. The attending physician had made some greasy applications and then had applied

yards and yards of bandage and enclosed the whole with oiled silk. On taking down this elaborate dressing the stench was almost intolerable, and the whole arm was in a state of intense edema, lymphangitis, and superficial gangrene. The second example refers to a gentleman whose skin was poisoned and subsequently, unfortunately, maltreated, so that eczema supervened, and the hapless victim was unable to attend his daughter's wedding more than a year later.

Before your patient leaves you warn him that for a few weeks the skin will be very susceptible to infection, and to cold, heat, and friction, for there can be but little or no horny layer on the affected parts. Also bear in mind that for a short period or for years the individual's skin has become sensitized to the original irritant and to its congeners. Let me illustrate this point as evinced in a recent case of bromin-poisoning. A lady presented a small but foul ulcer near the ankle. Ordinary antiseptic washes and ointments, even with rest in bed and elevation of the foot of the bed, made no impression on the sluggishness of the ulcer. An oily preparation of Dakin's solution was then applied, and almost immediately the size of the ulcer began to increase and the pain to intensify. In a casual remark the patient stated that she was taking sodium bromid from another physician! Here then was the effect of one irritating drug, chlorin, on its original congener, bromin. Both drugs were stopped, and the sloughing character and the rapid extension of the process ceased at once, and the wound progressed with gratifying celerity to a perfect healing.

DERMATITIS MEDICAMENTOSA

This subject is too large to describe in detail here, but nevertheless it is included in this survey of common errors because the general practitioner seems at times to fail to bear its possibilities in mind, and to ignore the fact that mother's milk may convey to the nursling the exciting drugs that she may be taking at the time. After listening to the above anecdote one might very properly accuse me of just this fault. The only excuse would be to say that the patient presented none of the

characteristics of chronic bromin-poisoning, *i. e.*, no mental torpor, no dull facies, no acneiform lesions of the face and shoulders, and no tendency in the ulcer toward papillomatosis. There seems to be only one sure road toward the mastery of this complicated and important chapter in dermatology. First, one must learn by rote the possible changes in the skin induced by the known mischief-making drugs; and second, one must recognize the fact that the objective lesions presented may not conform to those of other well-recognized diseases. Then one must begin to ask questions; but here again, as in dermatitis venenata, one must not be contented with "No" for an answer. Persistency must be our watchword. Some patients do not think; some don't want to, and others will deliberately lie.

DERMATITIS FACTITIA

Text-books are perhaps more apt to speak of this condition as malingering or again as hysteric gangrene, but the above title seems, on the whole, the best one. I shall try to make myself very emphatic and very explicit on this subject, for the errors I have seen committed in this disease, even by some of the best surgeons, can only be described as butchery, and, curiously enough, when the error has been pointed out to them they frequently refuse to believe one word they are told. The Skin Department of the Massachusetts General Hospital has a striking series of photographs illustrating what these patients have begun, and, in some cases, what too credulous surgeons have finished.

The only way to recognize this condition is: first, to appreciate that it exists; second, to be struck by the fact that its main features cannot be explained by ordinary disease; third, not to be led astray by sentiment or by specious arguments. Never mind if a schoolteacher tells you with tears in her eyes that she is poor and must return to work as soon as possible; never mind if a good-looking young girl has great ulcers on her breasts; never mind if a young girl has allowed one joint after another of a finger to be cut off; never mind if a woman has allowed tissue to be excised from her chest and abdomen to such

an extent that the resulting scars suggest nothing short of an Armenian massacre. Despite all these seemingly convincing arguments against what might be called common sense, don't waver when once you have made up your mind that dermatitis artefacta is present. Don't let even your elders persuade you from a proper diagnosis. Above all, pay no attention whatever to what the patient may tell you. These victims are practically always hysteric and may commit these self-mutilations in a subconscious state. These sentences may seem dictatorial, unsympathetic, arrogant; call them what you will. I can merely repeat that the Skin Department of the Massachusetts General Hospital has had a large experience in this condition and knows whereof it speaks.

DERMATITIS ACTINICA

As time goes on we recognize more and more fully the capability of good and of evil exercised by the Roentgen rays. It has been my privilege often to prescribe successfully the *x*-rays in the treatment of several obstinate dermatoses, but it has also been my lot to see the cruel results of too long and too frequent exposures to these same rays. Nowadays carelessness in screening and a too rapid repetition of the exposures usually produce the evil consequences. Quite a series of patients have consulted me for alopecia following the application of the rays to determine the presence or the absence of dental cavities. Far too great a number of luckless individuals have come to me for the treatment of *x*-ray burns of all degrees. Let me advise you, therefore, to test the susceptibility of each individual before undertaking any prolonged or repeated exposures; let me warn you to screen properly the actual focus and all surrounding tissue before turning on the current; let me, finally, ask you before making the exposure to remove with some solvent all grease from the skin, and not to use on the exposed surface any grease whatsoever for a period of ten days at least after the exposure. Grease beforehand materially alters the penetrability and the intensity of the rays; grease afterward, in case of hypersusceptibility or overexposure, materially "makes a bad job worse."

If a patient consults you for an *x*-ray burn, remove all grease at once, forbid its future use, and prescribe "white wash" (*vide* Erythema Multiforme), to be sopped on every hour, or whenever the pain demands it, and never bandage. Within a few days it will be evident whether or no you have a superficial and an amenable case to deal with. If the pain and redness and edema don't subside, if an ulcer is present or soon develops, don't waste another moment on external medication. There is only one proper and successful method of relief from the exhausting pain and the intractability of the lesion, and that lies in surgery—a wide and deep excision of the whole affected area and a subsequent skin-graft. Long experience has firmly convinced me of the truth of this statement.

LUPUS VULGARIS

Lupus vulgaris is not a common disease in New England, and yet it leads to no end of mischief in the hands of the medical unwary. In the Middle West and in California this disease is frequently confounded with blastomycosis and with oïdiomycosis. Clinically, we must bear in mind that the skin in blastomycosis is usually riddled with pus canals from which the yellow fluid can be easily expressed, and that its periphery is almost always of a marked purple hue. The similarity between lupus vulgaris, on the one hand, and blastomycosis and oïdiomycosis, on the other, however, may be so great that a resort to the microscopic examination of the pus and of the stained sections and even to cultural methods may be obligatory before a positive diagnosis can be made and accepted.

To the New Englander this differentiation is not the usual pitfall. The eastern medical man must be forever on his guard that he does not confuse lupus vulgaris with syphilis, and vice versa. It is no exaggeration for me to state that this unhappy mistake is not at all a rare occurrence, and this is especially true in the case of the nose; in truth, it seems at times as though certain practitioners could not be aware that there is such a condition as late syphilis of the nose. Syphilis of the nose is apt to be found after the age of thirty; as a rule lupus occurs in

childhood and in early adult life; syphilis presents a turgid red-blue color, lupus is apt to be a brownish red; syphilis is prone to appear as a rather homogeneous swelling; lupus usually presents one or more so-called lupus nodules; syphilis is less crusted than lupus; syphilis is more frequently accompanied by the odor of necrosis than lupus; there is more variation in the intensity of the syphilitic process; lupus is apt to run an unchanged course. I enter especially into these details because I have witnessed sad mutilations of this most conspicuous feature when a better knowledge of skin diseases, or a little more study of the individual case, would have enabled the practitioner to have administered salvarsan or iodid of potash and saved the integrity of the face. There are, of course, confusing examples of the two diseases in other parts of the body, but these mistakes are less disfiguring, although the consequences may be equally disastrous in the long run. Be on your guard, therefore, and remember the fact that these two diseases may often bear so close a similitude that serologic and therapeutic tests must be invoked before a final and definite conclusion can be drawn.

ERYTHEMA INDURATUM

This is a disease which is not as well understood as it should be, and when the physician is confronted with the one or more deep, subcutaneous nodules he is apt to consider the disease syphilis and to administer iodid of potash, a drug which usually causes a marked exacerbation of the hitherto sluggish condition. When called upon to diagnosticate this subvariety of tuberculosis remember that the gummata of syphilis when on the legs are apt to be single; to occur over some part of the front of the tibia; to arise with some rapidity; to appear in middle life or later, and to be asymmetric. Erythema induratum, per contra, usually presents several or more slowly evolving tumors, at first deep in the panniculus adiposus, and gradually extending to the surface; the nodules are on the back and sides of the legs and both legs are apt to be symmetrically involved; the patient is almost always a young woman and one in whom tuberculosis may be present. It will not be amiss to detail in this connection

a form of treatment which is but little known and has, as yet, found no place in the text-books. We owe this successful method of treatment of this hitherto intractable malady to Dr. F. S. Burns, of the Skin Department of the Massachusetts General Hospital. The procedure is simple and consists merely in the thorough curetage of each lesion down to the fascia, allowing the wound to granulate up from the bottom, with subsequent skin-grafting, if necessary. The operator will be struck by the depth and the extent of each nodule and by the unexpectedly short period of convalescence, granted that an abundance of fresh air and easily digested and nourishing food are obtainable.

SYPHILIS

Medical literature and personal experience are so full of errors in the diagnosis of syphilis that it seems hardly necessary to enter into details here. Suffice it to say that we must always be on our guard lest we confuse primary lesions with herpes progenitalis, "soft sores," carcinoma, felons, boils, and gummata. One is particularly liable to error in extragenital chancres, especially when near the finger-nails or on the tongue or the tonsil. In the early secondary stage of the infection we must not confuse the roseola with drug eruptions or the exanthemata or pityriasis rosea; nor the papular type with lichen planus, follicular eczema or dermatitis medicamentosa; we must not mistake hemorrhoids for condylomata; we must not call the patchy loss of hair alopecia areata; we must not fail to note the significance of mucous plaques. In the later seconday stages we must be very careful to differentiate multiple ringworm, psoriasis, and lupus vulgaris from the serpiginous types of the disease. In the so-called tertiary stage we must watch out that we do not mistake gummata for carcinoma, erythema induratum, or perhaps mycosis fungoides. In other words, throughout our whole career we must remember that syphilis is the great "imitator," and that if we cannot all have a special knowledge of skin diseases, we can at least own and become proficient in the use of the dark-field lens and in the taking of blood for the Wassermann test. These two procedures alone, if practised universally,

would eliminate the great majority of physicians' many errors in this truly large and important field of medicine.

TINEA TRICOPHYTINA

From a differential diagnostic point of view I have already spoken of ringworm under several previous headings; but there is one type of the disease which is but little known and which I have not mentioned, and that is the multiple purulent infection of the hairy regions. This infection is due to the variety of the ringworm plant known as the Megalosporon ectothrix—a variety derived from horses and from cattle. When this specific infection occurs in the scalp it is called kerion Celsi, and consists of a definitely round, sharply raised plateau, the surface of which is red and raw and riddled with holes (the hair-follicles) from which pus runs, or else is confined within a pustule. This phenomenon is known and recognized by a certain proportion of general practitioners, but its analogue in the beard seems to be but little known to any save the expert. In the beard the infection is not confined within any definite limits. The process is of very rapid evolution, and in the space of a few days the patient notes one follicle after another involved in intense swelling and inflammation and literally streaming with pus. Don't mistake this for an ordinary sycosis, it is not. Fortunately, a cure is not at all difficult, principally because the hair, the food of the plant, is detached from its papilla and is floated off in the stream of pus. Hot water fomentations three times a day and the inunction of the following ointment will bring about a cure within a few weeks:

℞. Beta-naphthol 2
Acid. carbol. 4
Sulph. flor. 4
Adipis benzoat. 30

Don't bandage.

From a therapeutic point it will not be amiss to emphasize here the great value of the *x*-rays as an epilating agent in the treatment of the ordinary ringworm infection of the scalp.

When we remember that cure of this trouble by our older methods necessitated exclusion from school for a period of six months and that it entailed the constant use of ointments we can well appreciate the boon conferred on school children and their parents by Sabouraud's introduction of the *x*-ray method. No tyro should undertake this work. The dangers of an *x*-ray burn or permanent baldness demand absolutely the expert's care in these cases. Few of us are experts in radiology, but that should not deter a single one of us from sending every case of ringworm to the expert, no matter how far away he may live, granted that such a procedure is feasible. One exposure suffices, provided that the infected area is not too large. Within three to six weeks new hair, free from the previous organism, begins to grow, and the child can then go to school. Remember the injunction about the use of any grease whatsoever within a period of ten days after an *x*-ray exposure. After this danger period apply twice daily to the affected surface the ointment recommended for the Megalosporon ectothrix (*q. v.*). These inunctions will keep down any possible superficial reinfection and will stimulate the growth of the new hairs.

KERATOSIS SENILIS

We are all familiar with the rough pigmentary patches on the face and on the backs of the hands of individuals. We must not confuse this disease with vitiligo, with chloasma, or with xanthoma—keratosis senilis is accompanied by hyperkeratosis. Nor must we exclude this diagnosis because the affected individual is still young or because he has not led an out-of-door life. The disease may exist in early adult life and even in "shut-ins." Let me ask you here not to waste time on ointments. They do not penetrate deeply enough to effect a cure. Radium or the more rapid curet plus subsequent cauterization are essential, and when properly used produce a permanent cure. As to our choice of procedure, remember that radium is less painful and will produce the better cosmetic results; but the curet is quicker and cheaper. Explain the alternatives and abide by the patient's decision. Before dismissing your patient explain fully

the etiologic effect of strong light on the development of future lesions, and tell him that before any prolonged necessary exposure to light in the future it would be well to cover the face and hands with "pink wash" (*vide* Pityriasis Rosea) in winter and "white wash" (*vide* Erythema Multiforme) in summer.

WARTS

Verruca Vulgaris.—It has been my lot to see a good many young people, especially girls, affected with warts—ordinary "seed warts." These patients ask what is the best form of treatment by which they may be rid of their disfiguring "blemishes." They very often say that they don't want any more warts burned out because the resulting scar is so ugly. This is the point I wish to emphasize. Don't burn warts with acids or the thermocautery, for the scars are ugly. In my opinion it is better to do nothing than to leave permanent disfigurement, which, after all, is not usually necessary, because warts on the hands will almost inevitably eventually disappear of themselves. Assuming that verruca vulgaris is produced by an animal parasite, an antibody is produced sooner or later which renders its life tenure impossible. Such a biologic phenomenon will properly explain the thousand and one "cures" for warts. However, the average patient does not care to be told by a physician to leave things alone. He consults a doctor because he wants positive help and action. What advice can one give, then? I believe we have a solution of this old question in the high-frequency machine, and, in my opinion, fulguration (as the method is called) in the expert's hands will practically always cure the disease within a reasonable time. Curiously enough, as you probably know, the operator does not have to electrocute every lesion, for after a certain number have been treated the remainder often suddenly disappear *en masse.* Here again antibodies are presumably at work.

This method of fulguration is especially useful in warts of the sole of the foot—hitherto a really serious therapeutic problem. Don't excise warts in this part of the body. Sterilization of the field of operation is peculiarly difficult; the procedure

is always temporarily crippling; and very often the wart returns.

Verruca Plana Juvenilis.—This is a variety of wart which is not well understood. It exists on the face and on the backs of the hands—exposed places—in the form of one or many, yellow-buff, or occasionally pink, flat-topped, squarish or oblong, smooth-surfaced, scaleless papules, which often occur in linear groups. These marked objective divergencies from other varieties of warts cause one to wonder why these tumors should be grouped under the general heading of verruca until we find that etymologically the word means an eminence. In the refinements of intricate diagnosis we must not confuse verruca plana juvenilis with some of the multiple benign cystic epitheliomata—syringoma or syringocystadenoma, for instance; otherwise bearing in my mind the position, the number, the color, the character of the top, the shape and the distribution of the lesions, the diagnosis is simple.

This not very common tumor has been included in this lecture because when present in abundance it may ruin temporarily a sensitive person's life, and because there is, in my opinion, a definite cure for it—a cure which has not yet been accepted by the text-books, but one in which we at the Massachusetts General Hospital have faith. This cure consists in the internal administration of the following pill:

℞. Hydrarg. iodid. virid..... 1
Ext. gentian..... q. s.—M.
Ft. pil. No. lx.
Sig.—For an adult, one pill t. i. d., p. c.

The disappearance of the warts, following the ingestion of these pills, may take place within two weeks, but more often the tumors are more obstinate, and in certain instances several months may be required to effect a cure. Don't lose heart under these circumstances. Be persistent, and in the end you and your faithful patient will be rewarded. During these weeks or months of mercurial ingestion never forget the strictest oral antisepsis.

Verruca Senilis.—This is, of course, a well-known variety of wart, but one which may require surgical interference. Tell your patients to watch these tumors, and if they grow unduly large or take on unaccustomed hyperkeratosis or bleed, advise radium, careful excision, or curetage and cauterization.

PRURITUS

Pruritus senilis is one of the banes of old age, but the well-informed physician can assure his patient a perfect cure. Innumerable applications have been recommended and usually in vain, for none are successful beyond a certain point. The *x*-rays, however, when administered by an expert in so-called analgesic doses, are invariably successful, and constitute, so far as I know, the only method of cure. Certain details of living will aid in this cure, and have been described in this lecture in connection with the paragraphs on winter eczema (*q. v.*). It is assumed, naturally, that a previous careful examination of the cardiorenal functions of the patient has been made.

Pruritus vulvæ and pruritus ani are likewise two great dermatologic problems. The solution of these vexing questions was never wholly solved in my opinion until the discovery of the therapeutic uses of crude coal-tar. Volumes have been written on the subject of the treatment of pruritus ani. Divers drugs, internal and external, have been tried and found wanting. Various operations have been described and performed, many times unavailingly. Elaborate physical examinations, never to be deprecated, of course, have been instituted, but usually without results. The cure, however, as hinted at above, is really very simple, and what I am about to describe is based on personal experience, even of desperate cases which have persisted over many years, and have defied the care of the most skilful physicians, surgeons, and proctologists.

In the case of pruritus ani it is assumed that personal hygiene to the uttermost will be explained and enforced. To be explicit, personal hygiene includes the maximum amount of fresh air and sleep; the proper proportion of work and play; the devotion of a certain amount of time to daily out-of-door exercise, according

to the age and ability of the individual; a daily bath of a temperature best suited to personal temperament; the ingestion of simply cooked, easily digested, well-balanced food, slowly eaten and followed by a half-hour of mental and physical relaxation; the avoidance of all stimulants, solid as well as liquid; and finally, the daily easy movement of the bowels. Such a regimen is a *sine qua non* to the best and quickest results.

The hygiene of the anus is of paramount importance. Experience has shown that pruritus ani is almost invariably accompanied by redundancy of the anal folds, and the depths and recesses of these folds serve as hotbeds of bacterial life, and consequently must play a decided rôle in the production and continuation of eczema and itching about the anus. Therefore we must counteract these mischievous anatomic defects as much as possible. Don't hesitate in this tormenting condition to go with your patient into the minutest detail of treatment. "The art of taking pains" should ever be a maxim with the dermatologist. After defecation the patient should remove the external fecal remainder with wet, thin toilet paper. He should then get into a squatting position on the floor with a good light and a mirror before him and should dry the anal region most carefully and thoroughly with absorbent cotton. Remember that heat, darkness, and moisture favor bacterial growth. Still remaining in this squatting position, with the mirror on the floor before him, the patient should apply to the interstices of the anal folds, by means of a fine cotton swab, a minimum amount of a 5 per cent. crude coal-tar ointment. The patient should not adopt a careless, forward and backward movement of the applicator, but should begin always at the lumen and paint outward to the periphery of the local pigmented area. The painting of the spokes of a wheel would be a somewhat similar proceeding, only in this instance we are painting in between the spokes. This maneuver should be performed morning and night, and before each fresh application the old ointment should be carefully removed with the oil of sweet almonds. Remember, as in all cases where crude coal-tar is to be used, to clip the neighboring hairs and keep them short.

Such is a successful method of treating pruritus ani, and, if pursued *in toto* by you and your patients, I believe will not often fail you.

This brings me to the end of what I want to say to you today. The omissions and commissions which I have endeavored to describe do not comprise single instances—they have been numerous. I have thought of them often and wondered how they could be avoided. For this reason I have come before you today, hoping by honest, constructive criticism to help you to avoid them in the future.

CONTRIBUTION BY DR. FRITZ B. TALBOT

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THE RELATION OF DIET TO THE DEVELOPMENT OF CHILDREN, WITH SPECIAL REFERENCE TO THE TEETH[1]

THE diet of the growing child and the proper digestion of the food is the most important single factor in considering the physical welfare of children. It is of importance also in dentistry, in that upon the general well-being of the child depends the health of his teeth and their proper development. This paper will deal more with the problems belonging especially to pediatrics, but problems which directly or indirectly have a bearing on the health of the teeth. In order to understand the rôle of diet in infancy and childhood a few general principles must be outlined.

The food is composed of fat, carbohydrate, protein, salts, and water. The fats and carbohydrates supply fuel to the body with which to keep it warm; the protein builds up tissues, the salts build up the skeleton and teeth; while water carries away the waste products and dissolves the solids.

The period of infancy especially and early childhood is a period of rapid growth. There is a great increase of all the tissues during this time to make this growth possible. The quality and quantity of the food plays an important part in obtaining proper growth and, therefore, must be considered in detail. This will be done later in this communication.

The protein needs are at least 2 grams of protein per kilogram of body weight. This amount of protein must be given

[1] Paper submitted to the Academy of Dental Science, Boston, Massachusetts.

in the diet so that there will be enough to form new tissues in muscles and organs. The adult differs from the growing child in that the adult requires only enough protein to replace that used up in the wear and tear of every-day life, while the child must have enough to replace wear and tear, and also a surplus to deposit in the body to supply the necessary materials for normal growth.

The metabolism of the salts is comparable to that of protein, in that in childhood enough salts must be present both to replace those lost during wear and tear and also to build up new tissue. The present knowledge of the metabolism of salts is very limited, but a few facts are sufficiently well established to be outlined here.

The inorganic constitutents of the bones make up 40 per cent. of the dry residue and the organic constituents 60 per cent. "The inorganic constituents are chiefly calcium phosphate and carbonate, but there is also a little magnesium and a trace of fluorids and chlorid" (Matthews).

The teeth are composed of cement, dentin, and enamel. The cement has the same chemical composition as bone. Dentin, which makes up the greater part of the teeth, also has the same chemical composition, although its structure is different. The enamel is the hardest structure in the body, and contains only 5 per cent. of water. In the human it is composed of 91 per cent. calcium phosphate. Calcium phosphate, therefore, is the most important single element in both the bones and the teeth, and it may be assumed also that anything that affected the one would also affect the other. In studying the diet and its relation to the teeth, the rôle of calcium phosphate in metabolism must be understood. It must be considered from the point of view of the metabolism as a whole and of the metabolism in diseases of the bony structure, such as rickets.

The calcium requirements of the body can only be determined by metabolism experiments in which the calcium in the food, urine, and feces is determined. The figures available are not numerous, but in man 0.4 to 1 gram of calcium oxid a day is required in the food to maintain an equilibrium, while a total

amount of 0.7 gram of calcium oxid a day is supposed to be a minimum. An infant should absorb at least 0.13 gram of calcium oxid in the day, according to Orgler, otherwise it will develop rickets. The average amount taken by all infants is between 0.17 and 0.18 gram per day. This amount, when compared to the adult requirements, is very high. The body weight of an adult is at least ten times as great as that of an infant five months of age, whereas his calcium requirements are only four times as great. If the infant were as large as the adult and still growing, it would require 2 or more grams of calcium per day to supply its needs. The high calcium requirement in infancy is, of course, due to the demands to make new bony structure. Before birth and during the months after birth, while the infant is nursed at the breast, the demands of the child are satisfied by the mother. Her calcium requirements are, consequently, increased, and unless extra lime is given in the diet to make up for this, her teeth and skeleton may suffer. This should be borne in mind by the dentist under whose care a nursing mother may come. After weaning, the supply of calcium to the child is not automatically regulated, and depends upon the person who prescribes the formulas which the infant receives.

The period of infancy is that of greatest growth. The body doubles its birth weight in the first five months and triples it in the first year. During that period the source of the food is principally milk, while in childhood a great variety of foods are given, and growth is not so rapid. It is during infancy when the commonest disease of the bones—rickets—is found. The results of rickets are seen in childhood, but a child rarely develops rickets after the second year. Since rickets is the disease most often associated with delayed dentition, it must be considered here. Rickets is characterized by having a deficient supply of calcium in the skeleton. This deficiency in calcium is explained by:

1. Poor hygiene and lack of exercise.
2. Abnormality of the glandular secretion.
3. Calcium starvation, too little in the food.

4. Withdrawal of calcium from the body because of faulty digestion or metabolism.

The effect of the organs of internal secretion, such as hypophysis, thyroid, ovaries, and testes, on the metabolism of calcium is so little understood that at present judgment must be withheld. The burden of proof lies with those who believe that these organs as a whole or singly have any influence at all. For practical purposes at present, at least, it must be assumed that they have no effect on the calcium metabolism.

Although poor hygiene and lack of exercise is usually present in rickets, sufficiently accurate data has not been gathered to prove that it is the cause. The writer believes that it is coincident, and that the cause should be sought in the diet.

Calcium starvation, or too little calcium in the food, is also quite unusual in early childhood or infancy, when the diet is composed in large part of milk. But all children do not drink milk, and it is more than possible that the diet may contain so little milk and other foods containing calcium that there is actually calcium starvation. When this is found to be the case, the diet should be so regulated as to supply enough calcium in the food, although inorganic calcium in water and lime-water can be absorbed as well as organic calcium. It is, however, in such small amounts that it is of no practical value. According to Sherman, "A quart of milk contains rather more calcium than a quart of clear saturated lime-water, and by far the most practical means of insuring an abundance of calcium in the dietary is to use milk freely as a food."

Calcium starvation, with the resulting diminished calcium in the bones, has been produced artificially in animals. This has been accomplished by feeding animals food deficient in calcium, on an acid food, or a combination of the two. After feeding animals for a period on such a food, they have become clinically rachitic, with enlarged epiphyses. The microscopic appearance of their bones differs from that of true rickets. The bones have a very low calcium content, but have not lost rela-

tively as much magnesium as is lost in true rickets. The following example from Rolopf shows how the bones of a growing puppy on a calcium poor diet differs from one on a calcium rich diet:

Diet.	Dry substance.	Ash.	CaO.	Phosphoric acid.
Ca poor shoulder-blade.....	2.678	1.178	0.638	0.499
Ca rich shoulder-blade.....	9.021	5.240	2.861	2.211

Unfortunately, similar observations and analyses were not made of the teeth, so that it will have to be assumed that what applies to the bony skeleton also applies to the teeth. The calcium content of the different foods will be given later and the diet commented upon. It will then be quite clear that with certain combinations of food a diet deficient in calcium is quite possible even in the diet of older children. During infancy this will not be possible when the food is made up of human or cow's milk except under unusual conditions.

Some other agent must, therefore, be a causative factor of rickets in infancy and later life. If there is sufficient calcium in the food, enough ought to reach the bones and teeth for normal growth. This does not always follow. The metabolism of salts is very complicated, but there seems to be enough evidence to conclude that certain abnormalities of digestion may so affect the absorption of calcium that even with enough in the food, rickets develops. This may happen when as a result of some abnormality of digestion or metabolism, more calcium is lost in the urine and feces than is taken in the food. An excess of fat in the food, for instance, may draw more calcium out of the body than was ingested in the food (Orgler). Carbohydrate may affect the calcium retention beneficially when given in normal amounts, and harmfully when given in enough excess to cause indigestion.

The following table, taken from Sherman,[1] shows the calcium content of the common articles of food:

[1]From Sherman's Chemistry of Food and Nutrition, page 290.

APPROXIMATE AMOUNTS OF CaO IN FOOD MATERIALS

Food.	CaO per 100 grams edible substance.	CaO per 100 grams protein.	CaO per 3000 calories.
Beef, all lean	0.01	0.045	0.25
Eggs	0.09	0.66	1.7
Egg yolk	0.2	1.3	1.6
Milk	0.17	5.1	7.2
Wheat, entire grain	0.06	0.4	0.52
Patent flour	0.025	0.26	0.2
Low-grade flour	0.04	0.3	0.4
Rice, polished	0.01	0.1	0.08
Oatmeal	0.013	0.008	0.1
Beans, dried	0.22	1.0	1.9
Peas, dried	0.14	0.4	0.9
Beets	0.03	1.9	1.9
Carrots	0.08	7.6	5.2
Parsnips	0.09	5.3	4.1
Potatoes	0.02	0.9	0.7
Turnips	0.09	6.9	6.4
Apples	0.014	3.5	0.6
Bananas	0.01	0.7	0.3
Oranges	0.06	7.8	3.4
Pineapples	0.02	5.2	1.4
Prunes, dried	0.06	1.8	0.6
Almonds	0.30	1.4	1.4
Peanuts	0.10	0.4	0.5
Walnuts	0.11	0.6	0.5

This table shows that beef, polished rice, and bananas are extraordinarily low in calcium; that the more highly refined wheat is, the less calcium does it contain. Milk, oatmeal, and beans stand out as containing large amounts of calcium, and obviously should be given in large amounts when it is desirable to feed more calcium to the body.

Phosphorus is necessary as well as calcium to form skeleton and teeth. It is deposited in both structures in combination with calcium, but in considering the diet it has not been considered separately from calcium. If it were necessary to consider phosphorus separately, the following from Sherman sums up the essential points to remember: "In general, the most practical and economic method of securing an abundance of phosphorus in suitable forms is by free use of milk, eggs, vegetables, and such cereal products and bread-stuffs as contain at

least a part of the outer layers as well as the inner portion of the grains."

The diet must be so balanced, however, that besides containing sufficient calcium it must also have enough calories for growth and enough protein to supply the needs of the tissues. It must be given in amounts that will not tax the digestion and be adapted to the needs of the individual child.

The diet of the infant that is so unfortunate as to be artificially fed belongs in the specialty of pediatrics. In early childhood breakfast should be composed of fruit, cereal, milk, eggs, or bacon. Dinner of meat or broth, one starchy vegetable, such as potato or rice, and one green vegetable, such as string beans, spinach or peas, with a dessert containing milk. Plain cheese, containing all the calcium of milk, should be used much more often than is the custom in this country. Supper should be simple, and consist of cereal and milk, or bread and milk, with some cooked fruit as a dainty.

Care of the bowels, mastication, and other good habits of eating will ensure a good digestion. These, with a proper diet, should ensure normal secretions in the mouth. It is advisable that a very young child should have a piece of dry toast or cracker to chew when the teeth have come through the gums, so that it will learn at an early date the habit of thoroughly masticating its food. Dry toast, baked in the oven, is especially good for this purpose, as it is hard and requires chewing and is also easily digested. It is my habit to give an infant a piece of toast to chew whenever enough teeth have erupted to give two biting surfaces.

There are many infants who do not cut their first teeth until the latter end of the first year, despite the fact that their diet is well regulated, and they have no evidence of rickets. Inquiry will usually elicit the information in these cases that this is a family peculiarity. Conversely, some infants are born with teeth.

There are no drugs known that will affect the growth of teeth. Rickets is said to be affected favorably by teaspoonful doses of phosphorus and cod-liver oil in the proportion of 1 : 3000.

The diet in later childhood depends upon the digestive capacity of the child. The most common errors of diet are to give too much sugar, sweets and candy, and too much fat. Sugar with every article of food is not necessary because it is converted into sugar before absorption. No child should receive more than one teaspoonful of sugar a day. Candy is bad for most teeth and should be strictly limited. The earliest symptom of too much sugar in the food is loss of appetite; the complexion becomes pale and muddy, the flesh flabby, and the abdomen often becomes distended.

Fat, when given in excess, may cause indigestion, with bulky, pale stools. These stools are composed almost entirely of fat. It has been shown that fat has the power of combining with the salts, including calcium, to make soaps. Enough calcium may be thus drawn from the body to result in a "negative balance," viz., more calcium is lost than is taken in the food. Although the gross appearance of the stools usually tells when there is an excessive amount of fat in the diet, it can sometimes only be determined by examination under the microscope. Cod-liver oil should not be given to such cases. The milk must be skimmed and the butter limited.

It is not necessary to emphasize the fact that no matter how good the diet, the digestion will not be good without healthy teeth and proper mastication. Improper diet, with unhealthy teeth, makes a vicious circle which will require time and careful treatment to cure. There are no principles of biologic chemistry which the writer is able to find which will explain the formation of tartar deposits on the teeth, and one must fall back on the general principles of dietetics and hygiene both of the teeth and the body to prevent its formation. These principles are well known and are based on experience.

CLINIC OF DR. CHANNING FROTHINGHAM

HARVARD MEDICAL SCHOOL

AORTIC ANEURYSM

An Example of Case Teaching at The Harvard Medical School, with Report of Autopsy

IN selecting cases for the course in case teaching for the third-year students at the Harvard Medical School those cases are chosen, in so far as possible, in which autopsies have been performed, in order that the case may be completely presented. The entire case, including history, physical examination, and clinical pathology, is presented in detail from the hospital record, and the various possible diagnoses recorded as they suggest themselves during the presentation of the case. After all the evidence has been presented, a discussion of the findings is held in order to select from the various possibilities the proper diagnosis. This is then confirmed or not by reading the pathologist's report. The case is then reviewed to emphasize the important points, or to endeavor to explain why any mistakes or omissions in diagnosis were made.

The case presented at this exercise is that of a man fifty years old, who, for the past five years, had been doing clerical work, although formerly he had been a grocer and bartender. He entered the hospital complaining of cough and difficulty in breathing and swallowing. The family history showed that his father died of locomotor ataxia at the age of seventy-five. His mother, brother, and two sisters are living and well. He has lost no brothers or sisters. There is a history of tuberculosis in one paternal uncle and of carcinoma in a maternal uncle.

He was married and lived with his wife for seventeen years, but they have now separated because of alcoholism on the wife's part. There have been no children or miscarriages resulting from the marriage.

The past history shows that he had measles, chickenpox, whooping-cough, typhoid fever, and scarlet fever in childhood. At eighteen years he was operated upon for a paraphimosis. At twenty years he had an attack of gonorrhea and has had three subsequent attacks, the last one when he was forty years old.

Since he was forty he has been bothered with hemorrhoids, which have at times bled considerably. He has noticed a slight increasing deafness for the past few years.

He has drunk a good deal of alcohol in the past, but usually periodically. He would drink 2 or 3 pints of whisky a day for a week and then would not drink any alcohol again for several weeks.

The family and past history in this case should call one's attention to certain points. Thus, the family history suggests as possibilities syphilis, tuberculosis, and cancer, although only rather remotely. The age of seventy-five is pretty well advanced for death from locomotor ataxia, and so some doubt would naturally be raised as to whether the father really died from that form of syphilitic infection. From the past history, one should bear in mind gall-stones as resulting from the typhoid fever, and possibly injury to the vascular system, endocardium, or kidneys as a result of the scarlet fever. Again, syphilis should be borne in mind from the repeated attacks of gonorrhea, as we know that such an infection is often coincident with a urethritis, and often overlooked. The possibility of cirrhosis of the liver should be suggested from the alcoholic history and hemorrhoids.

With these possibilities recorded, we turned to the present illness of the case. This started about two and a half years before admission, with pain in the right shoulder. The pain would come on while he was walking, and be relieved by lying down, or by supporting his right arm and shoulder. Associated with the pain was some numbness in his left hand, and shortness

of breath preceding the attack. For the past two and a half years he has been short of breath upon exertion, and would have to sit up often at night to breathe. During the past year the pain has also been present at times in his left arm, and also in his chest. This pain was sharp in nature, and would come and go, sometimes lasting as long as an hour. Associated with the pain in the chest he would sometimes feel quite uneasy and become blue in color.

During the past two and a half years he has had a very pronounced cough and has spit up a considerable amount of sputum. At this time he was suspected of having tuberculosis and recommended for treatment at the state sanatorium. He never spit up any blood until two weeks ago, when he raised a few clots of blood, but does not feel sure that they were not vomited rather than expectorated. About one year ago he began to notice that his voice became hoarse on exertion or when out in the cold. This has gradually become worse. During the past six months he has felt faint often, and once actually fainted on the street car. For the past two months he has noticed difficulty in swallowing. He finally gave up work one month before entrance to this hospital, and has been in bed most of the time with the disturbance to breathing and swallowing becoming progressively worse. During the past year he has lost about 60 pounds, most of it lately. Except for symptoms mentioned above he has no complaints, and his other functions are apparently normal.

The history of the present illness in this case directs our attention to the chest and mediastinum, and we find signs suggesting some tumor formation in the upper chest cavity which obstructs breathing and swallowing and causes referred pain in the arms. The tumor mass may be a begnin tumor, an aneurysm, a malignant growth, or enlarged glands associated with some disease. The possibility of the heart or kidneys or blood-pressure being at fault to account for the shortness of breath, and of some infiltrative process in the lungs to account for the cough must be considered.

The physical examination showed a well-developed, but

poorly nourished man who was conscious and clear mentally. He sat up in bed and, at times, exhibited some difficulty in breathing. His skull, scalp, hair, face, ears, nose, and skin presented nothing abnormal. His pupils were equal, regular in outline, and reacted to both light and accommodation. His eye-grounds were normal in appearance. His breath was foul, his teeth showed cavities, and there was pyorrhea and redness about the gums. His tongue was slightly coated and showed a slight tremor. The tonsils and pharynx were normal. His voice was husky, but the vocal cords could not be seen because the epiglottis obstructed the view and seemed to be paralyzed, as it did not move. In the neck there were no abnormal pulsations nor any enlargement of the lymph-nodes or thyroid. The lymph-glands throughout the body were not enlarged. The thorax was asymmetric, in that the left side was flatter than the right. On the left side expansion with inspiration was absent. No abnormal pulsations were seen.

The heart apex was palpable in the eighth left interspace in the posterior axillary line 23 cm. from the midsternum. There was dulness 2 cm. to the right of the sternal edge in the third and fourth spaces. On account of surrounding flatness in the left chest the left heart border could not be percussed. No thrills were felt on palpation. The heart sounds were regular, rapid, and of fair quality. Except for a soft systolic murmur heard only at the apex there were no murmurs. The aortic second sound was somewhat greater than the pulmonic second sound.

The left radial pulse was entirely absent, nor could any pulsation be made out in the left brachial artery. The right radial pulse was regular and of fair quality. The vessel walls were slightly palpable. From the left arm superficial veins ran across the front of the chest on the left side toward the ensiform region, where a large vein was seen running down the abdominal wall until it disappeared at the umbilicus. The blood in the superficial veins ran from above downward.

The blood-pressure was 115 systolic and 75 diastolic.

On percussion over the lungs the entire left side of the chest

front and back was flat, except from the angle of the scapula to the base behind, while on the right side there was hyperresonance. The lower border of the resonance in the right back descended well with inspiration. On auscultation the right lung presented normal breath sounds and no râles. The lower left chest, front, back, and axilla, presented markedly diminished breath sounds without râles. The tactile fremitus was also diminished. In front, from the left apex to the third interspace, there was distinct bronchial breathing without râles and with bronchial voice sounds, and over a corresponding area in the back there was distant bronchovesicular breathing without râles. Over the upper front the tactile fremitus in the left was increased, while behind it was much diminished. The abdomen was negative and the liver, spleen, and kidneys were not palpable.

The hands show some wasting of the muscles and a slight tremor, the left arm was colder and slightly more cyanotic than the right, and the veins on this arm were more prominent. Sensation to rough tests was apparently normal and the reflexes were present and equal on both sides.

On entrance the temperature was 99° F., the pulse 104, and the respiration 25. The urine showed the slightest possible trace of albumin and a few hyaline and granular casts. Subsequent examinations showed no albumin. The blood examination showed 100 per cent. hemoglobin, white count 19,400, with 90 per cent. of polymorphonuclear neutrophils. The stools showed no parasites, eggs, pus, or blood. The blood Wassermann was double plus. The electrocardiogram showed left ventricular hypertrophy, but otherwise a normal complex. The Roentgen report stated that there was a large uniformly dense shadow obscuring the entire lung field on the left and the outlines of the heart and aorta, except for a small bit of air-filled lung in the lateral aspect of the chest just above the diaphragm. There was no heart shadow to the right of the sternum and the trachea was displaced anteriorly. The findings suggested to the roentgenologist the presence of a neoplasm in the mediastinum. The mass which causes this shadow was rounded and smooth, but did not pulsate.

Of the possibilities suggested by the patient's history, it is possible now to rule out as a result of the physical examination and laboratory studies certain of them. Thus there is nothing to point to cirrhosis of the liver, as the liver is not palpable and there is no evidence of obstruction to the portal circulation. In fact, the enlarged vein in the abdominal wall suggests that the blood can reach the heart more easily from below. There is no evidence of any injury to the vascular system, endocardium, or kidneys referable to the scarlet fever, as the vessels are not palpably sclerosed, there are no important murmurs in the heart, the blood-pressure is not elevated, nor is there any evidence of nephritis. Against tuberculosis is the fact that although the signs in the left chest are extensive, there are no râles or evidence of pleural fluid. It would seem almost certain that so extensive a tuberculosis would be accompanied by râles. The location of the heart apex is doubtless due to the displacement of the heart, as there is no increased blood-pressure or valvular lesions to cause it to hypertrophy. Also the *x*-ray does not show the right border to the right of sternum as percussion suggested, so it presumably is not tremendously enlarged. Enlarged glands due to blood disorders are ruled out by the blood examination, and the limitation of the enlargement to this one area would be unusual in Hodgkin's disease.

Of the provisional diagnoses made, there remained, therefore, syphilis, which was confirmed by the Wassermann test, benign tumor, cyst, or malignant disease of the mediastinum, and gall-stones, which, of course, may be present, but which may be ruled out as being a factor of importance in the case. If syphilis is the cause of the signs and symptoms, it must be one of its end-results as an aneurysm, resulting from invasion and destruction of the medial count of the aorta by the spirochetes than a gumma, as the tumor mass is too large for that. Against aneurysm is the absence of pulsation on palpation or *x*-ray study, and the absence of tracheal tug and pupillary changes. In favor of aneurysm over benign or malignant tumor is the fact that it is more common than primary tumor in this region, and that a syphilitic infection is known to exist. The elevated tem-

perature and leukocytosis is more consistent with a tumor, especially a malignant one, than with an aneurysm. The disturbance to swallowing and breathing and the disturbance to the return of blood to the heart from above, as shown by the collateral circulation on the abdominal wall, simply mean pressure in the mediastinum upon the bronchi, esophagus, and superior vena cava or some other large vein, and do not help in differentiating between aneurysm and tumor. The emaciation does not help in the differential diagnosis, as it was obviously due to starvation dependent upon difficulty in swallowing. The notes in the record by the various doctors who examined the patient showed that difference of opinion existed among them in regard to the nature of the tumor mass.

The subsequent course of the disease showed that the patient was running a temperature which ranged from normal to 102.5° F. and a pulse which ranged from 85 to 120 per minute. The respirations varied between 20 and 30 per minute. The outstanding symptoms were pain in chest, dyspnea, and troublesome cough, from which only a thin watery sputum was raised. These symptoms required opiates frequently, and the difficulty in breathing became steadily more pronounced, until the patient practically choked to death three weeks after admission. During this period the leukocyte count continued elevated, but no other signs suggestive of any complicating disease occurred. Observation during these three weeks failed to add any further information to aid in differentiating between tumor and aneurysm.

The anatomic diagnoses made at autopsy were: aneurysm of the arch of the aorta, bronchopneumonia, gangrene of the lungs; posterior mediastinal abscess communicating with the esophagus, and fibrinopurulent pleurisy.

The pleurisy and bronchopneumonia were probably terminal affairs and did not exist at the time of admission. They probably contributed to the continued temperature and leukocytosis, but were not the original cause of it. The abscess in the posterior mediastinum probably was of slightly longer duration, and also helped to account for the leukocytosis and fever. The origin

of the leukocytosis and fever probably lay in the necrotic tissue caused by pressure from the aneurysm mass.

A clot was found extending into the left subclavian artery, which accounted for the absence of radial pulse on the left. Also in the aneurysmal sac there was much old clot, which probably accounted for the absence of pulsation in the fluoroscopic examination. The heart was apparently just crowded out of its normal position by the tumor mass, as was thought before death.

This case demonstrates the disturbance caused by a large tumor mass in the mediastinum, and reminds one that the usual signs, such as tracheal tug, pulsations, and bulging of the chest and irregularities of the pupils, may be absent in the presence of an aneurysm.

One should emphasize the fact that pain without apparent cause in the arms or chest or persistent cough without pulmonary involvement should always make one suspicious of the starting of trouble of a serious nature in the mediastinum.

CLINIC OF DR. GEORGE R. MINOT

MASSACHUSETTS GENERAL HOSPITAL

FOUR CASES WITH ENLARGED SPLEENS

Case I.—Banti's Disease. Discussion of Term "Splenic Anemia." The Symptoms, Blood-picture, and Differential Diagnosis of Banti's Disease. Splenectomy in Banti's Disease and Other Conditions.

Case II.—An Instance of Banti's Disease Mistaken for Peptic Ulcer. A Further Consideration of the Differential Diagnosis of Banti's Disease.

Case III.—Myelogenous Leukemia with a Low White Count. Illustration of the Value of Critical Blood Examination.

Case IV.—Typical Chronic Myelogenous Leukemia. Comments on Symptoms and Treatment by Radium.

I AM going to show you today four cases that have enlarged spleens, and I shall discuss their differential diagnosis and treatment.

CASE I

The first case is that of a boy aged fourteen, who gives the following summarized history:

Family history and *social history* entirely negative.

Habits good.

Past History.—He has never been "very strong" all his life. Tonsillectomy was performed when he was three years old. He had mumps at the age of five; measles at the age of seven; and pneumonia at the age of nine.

Present Illness.—When ten years old, now four years ago, he began having "indigestion attacks." These attacks consisted of a dull generalized abdominal pain, associated with some distention and belching of gas, lasting for a few days to two weeks. Sometimes accompanying this disturbance there would be nausea, rarely vomiting, and not infrequently diarrhea for two

or three days, with three to five stools a day. No blood was seen in the vomitus.

These attacks have persisted and increased in severity and frequency. At first they occurred every five or six weeks, but in the past year they have come at least every two weeks. During the past there has also been some gas and epigastric discomfort more or less continuously, with a poor appetite. There has been no sharp pain, no known fever, and these gastro-intestinal symptoms have rarely caused him to want to stay in bed.

During the past three years he has felt constantly tired and has grown increasingly weaker. Three years ago he weighed 59 pounds; a year ago, 62; and now, 59. Thus he is now much thinner than three years ago because he has grown several inches during this time.

Ten months ago he noticed his abdomen was abnormally large, and he thinks it has grown considerably bigger since then. His relatives state that he has been more or less pale for three years, and that he has been distinctly pale for a year, being paler now than a year ago.

During the past six months he has slept poorly, has had occasional headaches, and has been slightly short of breath.

Physical Examination.—Physical examination shows a pale, poorly nourished boy, with a large abdomen, and a few small purpuric spots on his legs. His temperature has been about 100° F. each evening for the past four days (since he has been under observation).

It is to be noted that it is not unusual for cases of his condition to have a degree or so of fever.

The pupils, throat, and mouth are negative. No lymph-nodes are palpable except for a few small pea-sized ones in the submaxillary and cervical regions.

The lungs are negative, and so is the heart, except for a slight functional systolic murmur.

The abdomen, besides appearing large and rather distended, shows slight tenderness in the epigastrium. The spleen is very much enlarged, reaching the midline at the umbilicus and ex-

tending 4 cm. below it in the left nipple line. It is very hard and firm, but not tender. The liver edge is easily felt 4 cm. below the costal margin, and is firm and non-tender. The upper border of liver dulness is at the sixth rib.

There is no jaundice and there are no dilated veins. There is no evidence of shifting dulness in flanks to suggest ascites. Neither kidney is felt. The genitals and reflexes are normal. The extremities are negative except for a slight clubbing of the fingers.

Though it is not usual to see clubbing of the fingers in the disease which this patient has, it may occur.

Laboratory Findings.—Urine and stool examination negative. Wassermann reaction negative.

Blood Examination.—Hemoglobin, 55 per cent.; red count, 3,300,000.

The *red cells* are achromic and show a definite abnormal variation in size, which is not marked. There are no very small red cells and no very large ones. There is only slight variation in shape. Rarely a polychromatophilic cell is seen. No stipling, Howell-Jolly bodies or blasts are present.

The *white count is 4000.* The differential count:

Polynuclear neutrophils	53	per cent.
Small lymphocytes	38	"
Large lymphocytes	3	"
Large mononuclears	6	"

No eosinophils or mast cells are seen.

Platelets are definitely considerably diminished in numbers.

Other blood tests revealed no positive information of value.

This case is a typical instance of *splenic anemia* in the stage of transition to the condition classically known as *Banti's disease.*

The term *splenic anemia* frequently has been used to include several distinct types of conditions, and its use should be restricted. Many types of conditions with enlarged spleens and anemia have been in the past called splenic anemia; I will refer to these later. The term *splenic anemia* is best reserved for the early stage of what is known as *Banti's disease;* or it may be bet-

ter to discard the term entirely and refer to such cases simply as Banti's disease in an early stage. The etiology and pathogenesis of this disease remains obscure. It usually occurs in young adults and runs a chronic course, being rather more common in men than in women. The disease is classically divided into three stages, which, of course, merge one into another, and are not in any given case sharply differentiated. Primary enlargement of the spleen is the first recognizable sign of the condition, and represents what is known as the first stage of the disease. This alone may be present for years. The second stage is associated with progressive enlargement of the spleen and anemia. The spleen is usually greatly enlarged, commonly reaching the umbilicus, and not infrequently being larger. As the anemia becomes evident, symptoms referable to it and to the enlargement of the spleen occur, such as increasing weakness, pallor, digestive disturbances, and abdominal discomfort; all of which symptoms are exhibited by this patient before you. It is to these first two stages of Banti's disease that the term "splenic anemia" is best applied.

As the disease progresses the third stage of this symptom complex, classically known as *Banti's disease*, occurs. In this stage the individual shows signs of cirrhosis of the liver and a failing portal dirculation, as evidenced especially by ascites.

The disease usually runs an extremely chronic course over a period of many years, and in some instances may never progress to the third stage; or it may rarely run a much more rapid course, so that the typical Banti's disease picture may be exhibited within perhaps a year. Though the disease is usually slowly progressive, there may be periods of remissions in the symptoms and the anemia. Such remissions are rarely very marked, and rarely if ever as marked as the marked remissions that may occur in pernicious anemia.

An important and frequent symptom that these cases often exhibit is hemorrhage from the gastro-intestinal tract. This is probably in many cases due to mechanical causes dependent upon the enlarged spleen, and in some instances from the cirrhosis of the liver. The bleeding may occur from gastric erosion

because of congestion, or from rupture of esophageal varices. Hemorrhages from other sources are not uncommon in these cases, particularly from the nose, as has occurred in the case before you. Such a hemorrhage often occurs without any clearly recognized defect of the blood factors associated with pathologic hemorrhage, and often without any recognized local mechanical defects.

Some cases, usually in the more advanced stages, do show a definite clear-cut hemorrhagic diathesis; a secondary purpura hemorrhagica. This is evidenced especially by spontaneous hemorrhages from the gums and nasal regions, and purpura, associated with marked diminution of the blood-platelets. The purpura on the legs of this boy is probably associated with distinct diminution of platelets in his blood.

Another factor that may be responsible for some of the pathologic hemorrhages is defective liver function. In some instances probably pathologic blood defect helps to exaggerate the gastro-intestinal hemorrhages largely dependent upon mechanical causes.

The defects of the hemopoietic organs in this disease would appear to be particularly *impaired blood formation*, but of a relatively normal type in contrast to that of an abnormal type seen in pernicious anemia. There also appears to be present sometimes some increased hemolytic activity. This is never marked.

The evidence of impaired blood formation is reflected in the peripheral blood-picture by a leukopenia, with not infrequently a relative lymphocytosis and absolute diminution of the polynuclear cells; diminished numbers of platelets, and red cells of a type seen in so-called chronic secondary anemia, with little evidence of their active regeneration. Leukopenia is a feature of the condition. The white count in uncomplicated cases when the disease is well established is probably never over 7000; usually about 3500. Following a severe hemorrhage the count may rise, but proportionally not so much as after a similar amount of hemorrhage from accident in a healthy person. Similarly, other complications may temporarily increase the

count. The red-cell picture in these cases, in the absence of complications, is as stated: that of chronic secondary anemia with a relatively lower hemoglobin than red-cell count; rarely do the cells vary greatly in size or shape; and though polychromatophilia and stipling may occur, they are practically never marked, nor are the reticulated red cells ever increased more than slightly. Apparently, relatively early in the disease, even though the spleen may reach the umbilicus, there may be evidence of a more active marrow, so there will not be a leukopenia, and the white count may rarely be as high as 10,000. Under such conditions the polynuclears may form a relatively high percentage (70 per cent.) of the white cells, and the "large mononuclear" cells are often increased. It is perhaps not uncommon to see the "large mononuclear" cells increased even with the lower white counts, and sometimes they appear in character somewhat different from those usually seen in normal bloods. With the higher counts an occasional polynuclear eosinophil or mast cell may be found; these are seldom found with the lower counts. Under such circumstances the red cells may show relatively more signs of youth, and the platelets, too, may be slightly increased, and not infrequently large in size.

The evidence of hemolytic activity, increased blood destruction, is particularly seen in increased excretion of urobilin and by increases of bile pigments in the plasma. This apparently is never marked, and does not occur early, and not infrequently is absent. The increase of bile pigments in the plasma is at times undoubtedly dependent upon the liver cirrhosis. Definite jaundice is never marked and is rare in the disease, probably not being seen until cirrhosis develops.

It is quite probable that the spleen normally has a regulatory action over the marrow, and it would seem that in this disease the altered splenic function was of such a nature that it caused an abnormal depression of the marrow without any marked alteration of its character. Perhaps early in the disease, or at times of remission, the marrow is able to overcome this depression. This impaired blood formation is probably the chief hemopoietic defect. As increased red-cell destruction is not

marked, it seems it must play a relatively small rôle in the production of the anemia.

Differential Diagnosis.—Among the conditions that in the past have been called splenic anemia, and which are to be distinguished from Banti's disease, are Gaucher's disease, von Jaksch's anemia, and the various types of hemolytic jaundice.

Gaucher's disease is characterized pathologically by a peculiar large vesicular cell hyperplasia of the spleen, while the spleen of Banti's disease shows chiefly simply increase of fibrous tissue. Gaucher's disease is much rarer than Banti's disease. The blood-picture may apparently be the same as in Banti's disease. The condition often is not recognized in life. The following points are unlike what occurs in Banti's disease and help to distinguish Gaucher's clinically. It begins insidiously in childhood; a family history is often elicited; the spleen reaches enormous proportions; and the liver is often large.

The condition known as *von Jaksch's anemia*, or anemia infantum pseudoleukemia, is a symptom complex that occurs in infants and children and not in adults. This has been well discussed by Stillman in The American Journal of The Medical Sciences (1917, vol. cliii, 218). It is characterized by marked enlargement of the spleen, with slight enlargement of the liver, and sometimes with enlargement of the superficial lymph-nodes. The blood-picture shows an anemia with a low color index, and a persistent leukocytosis of varying degree. The platelets are increased. Nucleated red cells are nearly always present, frequently in large numbers, and the red cells often show a lot of polychromatophilia and stipling. These features of the red-cell picture are in contrast to that of Banti's disease, as are the white-cell and platelet pictures. This type of anemia is very frequently associated with rickets, and sometimes with syphilis, although it may occur without association with either of these diseases. Exactly what relation the symptom complex has to rickets or syphilis has not been definitely decided. It has been thought by some that this condition is simply the form of Banti's disease that occurs in the infant. However, it seems more likely that it is not. Cases of von Jaksch's anemia tend to

recover; in contrast to cases of Banti's disease, which tend to progress.

The acquired and familiar forms of *hemolytic jaundice*, characterized by constant increased blood formation in the presence of constant increased blood destruction, with enlargement of the spleen, may present many variations from their typical picture. Such variations may be dependent upon fluctuations of the anemia and the degree of activity of the hemolytic organs, and the progressiveness of any given case. These cases have been called to our attention particularly in recent years, and in the past have not infrequently been called splenic anemia. The severest cases of the acquired type appear to approach in character the more chronic hemolytic type of pernicious anemia cases with enlarged spleens. I shall mention some points by which hemolytic jaundice may be distinguished from Banti's disease. A family history may be obtained in the familial form; the individuals in this group are not so sick as in the acquired form; in fact, some cases remain for life in fairly good health; and, as Chauffard has said, the familial cases are more icteric than sick. Cases of hemolytic jaundice are nearly always more chronic, not infrequently much more chronic, than Banti's disease. Definite jaundice without bile in the urine is nearly always to be seen, while it is relatively rare in Banti's disease. This jaundice is dependent upon a marked increased blood destruction. The spleen on the average is not so large as in cases of Banti's disease. The histologic blood-picture of cases of hemolytic jaundice shows evidence of increased marrow activity which is often marked, in contrast to the decreased marrow activity usually seen in Banti's disease; one of the features of hemolytic jaundice being increases, often marked increases, of the reticulated red cells. Another feature is the typical diminished resistance of the red cells to various strengths of salt solutions, which is not present in Banti's disease.

Among other conditions not to be confused with *Banti's disease* are cases of pernicious anemia with enlarged spleens, certain ill-defined types of hemolytic anemia, the leukemias, polycythemia vera, various types of cirrhosis of the liver, splenic

enlargements associated with sepsis, malignant endocarditis, malaria, kala-azar, etc., as well as Hodgkins' disease and its allied conditions with enlarged lymph-nodes. Two other conditions, different and at times impossible to differentiate from Banti's disease, are thrombosis of the portal and splenic veins and syphilitic splenomegaly. It will not be possible to discuss all these conditions, and I will simply briefly refer to the last two.

Thrombosis of the splenic vein may give the same symptomatology and apparently the same blood-picture as Banti's disease. It is often impossible to differentiate splenic enlargement secondary to thrombophlebitis from that due to Banti's disease. Also it is to be noted that probably in some cases of true Banti's disease thrombosis of splenic, portal, and mesenteric veins may occur secondary to it.

Syphilis may cause anemia with non-gummatous, diffuse hypertrophy of the spleen, and much more rarely gummata in the spleen. In fact, it may be only because the Wassermann reaction is definitely and strongly positive that such instances can be distinguished from Banti's disease. Perhaps some such cases are simply instances of Banti's disease occurring in a patient who has had syphilis. One can always speculate in such instances on what relation the syphilis has to the splenic enlargement. It does, however, seem quite proper to separate from the other forms of splenomegaly those cases with large spleens in which a syphilitic cirrhosis of the liver exists, and where gummata of the liver are present. It is quite possible that such cases may show a rather different blood-picture than true Banti's disease, but this has not as yet been clearly demonstrated.

Treatment.—The only method of real therapeutic value in Banti's disease is *splenectomy*. Temporary improvement may be obtained by purely medical methods, such as proper feeding, rest, fresh air, iron, etc. Roentgen rays or radium in some instances—probably particularly in early cases—may cause some decrease in the size of the spleen and permit temporary improvement. In many cases it is without significant effect. This procedure may be tried before surgery, with a view to allowing the patient to be in the best possible condition for operation.

The question of such a procedure causing adhesions and making the operation more difficult has been discussed in the literature, and it would seem that it probably did not cause any serious adhesions in such cases. When the diagnosis is definitely established, splenectomy should not be done too hastily. Simple measures, besides radiation, perhaps, should be first undertaken, in order to have the patient in the best possible condition, and the most favorable time should be selected for the operation. Transfusion may be indicated in certain cases to improve the patient's condition before operation. In all cases before operation it is desirable to have an appropriately selected donor at hand, so that transfusion can be done after the operation if necessary.

In those early cases where the spleen is not very large and where the disease is apparently rather stationary and the patient in very fair health, it is most difficult to say that splenectomy should be urged, because some such cases may remain for years quite well. However, with any evidence of progress of the disease, splenectomy should be urged. Probably it would be wise to urge removal of the spleen in all cases where the diagnosis is definitely made after careful study of the case.

The earlier in the disease the operation is done, the better the results, and the more lasting the improvement of the symptoms. In many cases in the first and early second stage operation amounts to a complete cure. When the third stage is reached the operation is by no means contraindicated, but the chances of improvement are greatly lessened. The operation in this stage is also more dangerous. The operative mortality in the recent essentially unselected cases of Banti's disease is in the vicinity of 12 per cent. With selected cases and early cases the mortality percentage is apparently considerably reduced. Some cases operated when ascites was present have improved markedly; such cases, however, are apt to die within a few years. Though many of the cases operated upon in a relatively early stage of the disease appear to be completely cured, others may live for many years, feeling quite well, and then suffer a relapse, the postmortem examination showing changes asso-

ciated with cirrhosis of the liver and progress of the disease process.

Splenectomy is often a desirable therapeutic measure *in* some of the *conditions* that may be *mistaken for Banti's disease.* It may be advised in Gaucher's disease, but in such cases its benefit is probably never as permanent as in Banti's disease, and not infrequently gains little for the patient. In hemolytic jaundice in the acquired or familial form splenectomy is to be advised provided the patient's symptoms are bothersome enough to handicap his health, or there is evidence that the condition is progressive. In those mild familial cases where the patient has nothing to complain of except his appearance, it does not seem wise to advise operation. The results in hemolytic jaundice conditions are usually very successful; marked improvement is the rule, but apparently cure is not universal. Relapses may occur after splenectomy. If it were not for the risk of operation, probably all cases should be splenectomized as soon as the diagnosis is made; and undoubtedly the earlier the operation, the better the results. However, it must be remembered that in spite of the very brilliant results the exact cause of the condition is unknown, and although the spleen appears an important pathologic element in the disease, probably the true disease process does not reside wholly in the spleen, as is probably also true in Banti's disease.

Splenectomy in von Jaksch's anemia has seldom been done, and it seems that it should be reserved only for cases resistant to prolonged careful medical treatment, for such treatment often yields satisfactory results.

In pernicious anemia, splenectomy is at the best only a palliative measure, and probably is not to be advised in the vast majority of cases. It seems to be the means for inducing as good a remission as possible, but the gain to the patient is often slight when compared to the discomforts and risk of the operation. In selected cases it may be advised, if not urged. The cases that do best seem to be those with enlarged spleens without acute onset and with evidence of a good deal of hemolysis with an active marrow.

In typical myelogenous leukemia splenectomy is never to be advised; in fact, it is distinctly contraindicated, as it usually results in death. Recently at the Mayo Clinic, following radium therapy with shrinkage of the spleen, splenectomy has been practised, but the results would seem to show that though the mortality from operation is vastly lower than in untreated cases, the ultimate result gains nothing more for the patient than radium alone. It is possible that in certain rare cases of chronic myelogenous leukemia with a relatively small spleen and a low white count splenectomy may be done to advantage. However, reports on such cases are meager, and we do not really know how much is to be gained in such cases by this procedure over that which may be accomplished by radiation of the spleen. It is, I think, rather doubtful if splenectomy in such cases will do more for the patient than frequent, carefully given treatments with radium.

True syphilitic splenomegaly with secondary anemia is often resistant to antisyphilitic treatment, and in such cases splenectomy has been advised by Giffin, and seems justifiable and desirable when other forms of treatment have failed.

In other forms of splenomegaly than those just discussed splenectomy should seldom be done, and if so, only in certain unusual and atypical cases.

CASE II

The second case that I have to show you illustrates an instance where hematemesis was thought to be due to peptic ulcer, and where, in fact, it was, in all probability, dependent upon mechanical vascular disturbance from an enlarged spleen in a case of Banti's disease.

The patient is a man of thirty-four, who has been a New England farmer all his life. His history is as follows:

Family history, social history, and *occupational history* are wholly negative.

Past History.—As a child he had measles and whooping-cough, and rarely a mild sore throat. Ten years ago he had a septic hand. There is no history of any symptoms referable to

any of the systems of the body until nine years ago. There is no history of malaria, venereal history, or typhoid.

Habits.—Rarely has he taken any alcoholic drinks. He has never smoked or chewed tobacco. His living conditions have been good, and he has eaten in no abnormal manner.

Present Illness.—(As the history is a lone one, I shall not give every detail the patient described, but will try to point out the salient facts.) Nine years ago he began having indefinite abdominal discomfort associated with the belching of a good deal of gas. This discomfort did not occur at any regular intervals in the day, but he thought he belched more gas in the mid-afternoon than at other times. After some weeks he began having typical "heartburn," beginning usually two hours after eating and lasting for about an hour. There was no vomiting, rarely nausea. After some months of these symptoms he developed suddenly, one night, sharp pain, which he now says occurred in the epigastrium. He recalls no details about this attack, but was operated upon for appendicitis, and was later told that the appendix was found "pretty normal." Following the operation his abdominal symptoms subsided for some weeks, but then recurred. They became even more marked than before, and not infrequently he had sharp attacks of cramp-like abdominal pain of hours' duration on the right side of his abdomen, usually associated with vomiting, but occurring without relation to food or posture. These attacks continued until about a year after his appendix operation, when he consulted different doctors than formerly. They advised operation for "adhesions." This was done, and he says adhesions were found. Following this, he had no return of the right-sided abdominal pain, but the heart-burn occasionally recurred, and general abdominal discomfort continued.

For the next two years the symptoms fluctuated in periods of weeks, during which time he found he had fewer symptoms if he did not eat coarse foods or fried foods. Then, instead of having general abdominal discomfort, he began to have epigastric distress and a dull epigastric pain, particularly two hours after eating; this was associated with increase of "heartburn"

and gas. After some months of this, or now about five years ago, one day he suddenly vomited at least a pint of blood. In the next eight months his symptoms of "heartburn," gas, and epigastric distress continued, but he considers he had no more real epigastric pain. During this period he vomited blood at least five times. His friends state that he had been growing pale for a year before his first hemorrhage, and that he has been more or less pale ever since then. A diagnosis of peptic ulcer was made by his doctor at this time, and a gastro-enterostomy was done. He says he was told that two very small superficial erosions were found on the stomach. At this time he first knew that his spleen was enlarged, and he claims he was told that it had enlarged because it was nature's way to stop his hemorrhages. The facts are, of course, that its enlargement was responsible for his hemorrhage.

In the next two and a half years he had no hemorrhages, but the hyperacidity symptoms, gas, and epigastric discomfort continued, with rarely nausea. These symptoms perhaps were not so marked as in the eight months preceding the gastro-enterostomy. Following this operation, his color definitely improved somewhat, but he remained rather pale. During these two years he had a few slight nose-bleeds; and in the past three months he has had several more.

Six months ago, at a time when he was having relatively mild stomach symptoms, he vomited about a quart of blood. Since then he has vomited only six times, but each time there was about half a pint of blood. During these past six months epigastric discomfort has been prominent, occurring more or less persistently.

During the past nine years his bowels have been fairly regular except in the past six months, when they have been distinctly constipated. This may be dependent upon the fact that he has taken a lot of iron during this time. Hemorrhoids have been present for at least five years. In the past six months he has had numerous symptoms, evidently dependent upon his anemia *per se;* such as weakness, dizziness, slight swelling of his ankles, and palpitation. He has lost about 25 pounds in

weight during the past six months, so that he now weighs 105 pounds. Ten years ago he weighed 150 pounds, and fluctuated between 140 and 125 in the first eight years of his illness. This recent loss of weight can be accounted for by the fact that he has eaten very little food in recent months because of being allowed but little on account of the hematemesis. He does not know whether his spleen has grown bigger or not. He is inclined to believe it is the same size now that it was four and a half years ago, when it was first called to his attention.

Physical Examination.—The patient is thin and pale—a white pallor and not at all sallow or yellowish, as is so commonly seen in cases with some form of hemolytic anemia. His temperature has been normal during the three days that he has been in the hospital.

The pupils react normally. Tongue, throat, tonsils, and teeth are negative. No lymph-nodes are palpable except for some tiny ones in the neck. The lungs are absolutely negative.

The heart is negative except for a soft but rather loud systolic murmur heard over the pericardium, but loudest at the base. This is, of course, a functional murmur dependent upon the anemia. The pulse rate is 80. The blood pressure is: systolic 110; diastolic 75.

Examination of the abdomen shows that there is a fulness in the left upper quadrant. No superficial veins are to be seen that are definitely abnormally prominent. Palpation of the abdomen reveals definite tenderness in the epigastrium, but not elsewhere. There is no distention and no evidence of ascites. The spleen is very easily felt and extends, on deep inspiration, to just above the level of the umbilicus. At first one is inclined to believe the spleen is not very large, but upon palpation you will note that though it does not come within 6 cm. of the midline, it fills the left flank, and percussion shows it to extend under the ribs even higher up and further back than normal. It is a pretty big spleen. It is very firm and hard, and the notch is easily felt. The liver edge can just be felt on deep inspiration. Neither kidney is felt, and no other tumors are felt.

Rectal examination reveals some external and internal hem-

orrhoids. The genitals and reflexes are negative. The extremities are negative except for a very slight edema of the ankles.

Two *Roentgen rays* of the gastro-intestinal tract have revealed no abnormality except the gastro-enterostomy stoma. Roentgen ray examination of the kidney and gall-bladder regions was negative.

Laboratory Examinations.—Two stool examinations have been negative. Two urine examinations are absolutely negative except for the slightest possible trace of albumin.

The Wassermann reaction of the blood is negative.

The *blood examination* is as follows:

Hemoglobin, 45 per cent. Red count, 2,800,000.

The *red cells* are distinctly but not markedly achromic. They vary considerably in size, but no true microcytes are present. There are no true macrocytes. Variation in shape occurs, but is not so marked as variation in size, and there are no very bizarre-shaped cells. Polychromatophilia rarely occurs. There is no stipling and no Howell-Jolly bodies, or blasts occur. The reticulated red cells are 1 per cent.

The fragility of the red cells shows that hemolysis begins in 0.42 per cent. salt solution, is marked in 0.36 per cent., and complete in 0.28 per cent. This is within the normal limits, but one might expect in an individual who has had so much hemorrhage that the hemolysis would be complete in a weaker percentage of salt solution.

The *white count is 2300.* The differential count of 200 cells is as follows:

Polynuclear neutrophils	51	per cent.
Small lymphocytes	44	"
Large lymphocytes	1	"
Large mononuclears	4	"
Eosinophils	0	"
Mast cells	0	"

The *platelets* are definitely somewhat diminished.

The bleeding time is not prolonged. Coagulation time is normal and the clot retracts. The serum shows no evidence of containing abnormal amounts of bile pigments.

The presence of the enlarged spleen with leukopenia *in the presence of anemia taken together with the repeated hematemesis and the nine-year history makes, without doubt, the diagnosis of Banti's disease.* It is surprising to note that the patient states that he has never had his blood examined until now, although he recalls seeing twelve different doctors in nine years. Of course, any one doing good medical work should study the blood in any case with a large spleen or one showing pallor. The case further serves to point out the importance of studying all cases very carefully before operations are performed. It is probable that five years ago, when the spleen was known to be enlarged, the blood would have shown essentially the same features as now. Directly after a hemorrhage there may have been a leukocytosis, so that a count at such a time would not have been so valuable as counts some ten days or so afterward. In the chronic anemia resulting from hemorrhage, as in simple duodenal ulcer, the white count will remain somewhat above normal, so that the presence of leukopenia in such a case—as in the one I have just described—would be alone very suggestive of splenic anemia rather than only peptic ulcer. It is true, of course, that the symptoms the patient had suggest peptic ulcer, and that two small gastric erosions were said to be found at operation. However, such lesions and symptoms highly probably resulted from the splenic condition, and treatment should have been directed not at the result, but at the cause; by which I mean the spleen should have been removed, and not a gastro-enterostomy done. If this had been done, the patient probably would be vastly better than he is now. It is most unlikely that all the hemorrhages this patient had came from small gastric erosions. The greater amount of blood highly probably came from ruptured esophageal varices. Not only does the nature of the case suggest this, but the negative gastro-intestinal Roentgen ray examination favors this assumption.

The mistake made in diagnosis which this case illustrates has been made before by excellent men, and reports of other such cases are to be found in the literature. I have seen the mistake made several times. In the other cases the spleen was

not quite so large; and in one it was unusually difficult to feel, yet after its removal it was found to be fully three times normal size.

Individuals who have enlarged spleens from malaria, etc., occurring in the past, at the time they are seen, of course, may have peptic ulcer, and such cases may be confused with Banti's disease. It is in cases with the smaller spleens that the diagnosis is difficult; and in such instances one has to rule out not particularly peptic ulcer, but ordinary *atrophic cirrhosis of the liver*, because this condition often gives slight or moderate enlargement of the spleen and recurring hematemesis from esophageal varices. The salient points to differentiate between these two conditions consist in obtaining a history of alcoholism and evidence of late and not early splenic enlargement, which favors cirrhosis and not Banti's disease. A large spleen will always be much in favor of Banti's disease. With *Banti's disease* there usually will be a longer history of anemia than in cirrhosis, and in this latter condition there is not much anemia except in the terminal stage or after profuse hemorrhage. The blood-picture may help to differentiate the two conditions, but cirrhosis of the liver in its later stages may show a leukopenia. At times it may be impossible to distinguish these two conditions, particularly when they are in the advanced stages.

About two weeks after removal of the spleen in this case (Case II) the patient died from mesenteric thrombosis. Autopsy showed most extensive varices of the esophagus. There was a relatively small amount of cirrhotic change in the liver, and no ulcers or scars were found in the stomach.

CASE III

The third case that I have to present is an instance of where the diagnosis is established by careful examination of the blood. I will present the case briefly to you.

The patient is a man of forty years, who has always done clerical work.

The *family history* is unimportant.

His *habits* are good.

The *past history* is negative except for the fact that he has had migraine all his life.

The *present illness* is of about a year's duration, though he doesn't consider that he has been really ill for more than two months. A year ago he first began to have "dyspepsia," which has persisted and increased up to the present time, particularly in the past two months. This has consisted of frequently belching gas, a dull indefinite mild ache in the epigastrium, occasional nausea, and heart-burn. There has never been sharp pain or vomiting. During this time the bowels have been constipated. Four months ago he began having a dragging pain in the region of the left flank, accompanied by a dull ache in the small of his back. These sensations have been aggravated by increase of gas and by exercise. They have never been present when he lies down.

In the last six months he has become fatigued unusually easily, and he has in general felt weak and used up, even though he went on a long vacation two months ago. This sense of not feeling well and of being weak and tired has increased, particularly in the past month; though he has attended to his business, he has felt mean enough to want to go to bed directly after his evening meal. He now weighs 145 pounds, having lost 10 pounds in six months. Four months ago his friends said he looked pale, and he is sure that he is paler now than a year ago, but he doubts if he is any paler than four months ago. There have been no other symptoms.

Physical Examination.—The patient looks a trifle pale and appears tired. The complete examination is entirely negative except for the abdomen.

The abdomen is not tender anywhere. The lower border of the spleen is easily felt with the patient breathing normally 2 cm. above the level of the umbilicus; it extends 6 cm. below the costal margin in the left nipple line, and is 3 cm. to the left of the midline at a point 4 cm. above the umbilicus. It is hard, though it does not feel so hard as the spleen of the last case I showed you. The liver edge can be easily felt descending 1 cm. below the costal margin on inspiration. No other organs

or masses are felt. There is slight tenderness over the left lumbar muscles.

The left-sided pain and backache that the patient complains of are probably caused mechanically by the weight of the spleen.

All laboratory examinations are negative except for that of the blood.

The *blood* has been examined several times in the past two weeks, and has always shown essentially the same findings. The *red count* is 4,800,000 and the *hemoglobin* 80 per cent. The *white count* fluctuates between 13,000 and 18,000. In the *routine report* the red cells were noted as simply showing slight variation in size, and the platelets as about normal in numbers. The differential count was given as follows:

Polynuclear neutrophils	60 per cent.
Small lymphocytes	17 "
Large lymphocytes	4 "
Large mononuclears	19 "

From this report one learns nothing that definitely suggests what the condition really is. It was thought by some at this time that the case was one of early Banti's disease. This, however, may be essentially ruled out by the elevated white count alone. The elevated white count in the presence of an enlarged spleen, with a report of *19 per cent. mononuclear* cells, should make one suspicious that the reported large mononuclear cells may have been mistaken for some abnormal mononuclear cells. Such is the case in this instance. When this patient's blood was *critically examined* it was found that the differential count was essentially as given (0.5 per cent. eosinophils and 0.5 per cent. mast cells did occur), but that the 19 per cent. large mononuclear cells were nearly all abnormal mononuclear cells. About 8 per cent. were clear-cut definite *myelocytes*, though their granules were often finer than the usual text-book myelocytes; 3 per cent. were probably normal large mononuclear cells. The other 8 per cent. were cells that looked at casually appeared like certain normal large mononuclear cells. I am unable definitely to name these cells, but will say that they were large mononuclear

cells abnormal in the peripheral blood, and that they gave the oxydase reaction, showing they were of myelogenous origin. They varied in size from that of a polynuclear to over twice this size. Practically all had dark large vesicular nuclei, at times double. Their protoplasm often curled and contained fine granules, and often quite coarse ones. Sometimes the granules were short and rod shaped. These cells were highly probably some form of myelocyte. Rarely a very large mononuclear cell occurred with intensely deep blue protoplasm. The lymphocytic cells not infrequently showed some immature forms. The polynuclears were sometimes abnormally large, and again abnormally small, not infrequently containing single-lobed nuclei.

From this white cell picture alone one should realize that he is probably dealing with *an instance of myelogenous leukemia* in a stage where the total white count is but slightly elevated. Further evidence of this is suggested by the *red-cell picture*. The red cells at a first glance are not at all striking, but when more critically examined one is impressed with the amount of abnormality they show, particularly when one considers the high level of the hemoglobin and red count. There actually occurs a definitely abnormal variation in size; occasionally a real microcyte is seen. No real macrocytes occur or deeply stained red cells. There is slight achromia. Variation in shape occurs, but is relatively slight. However, at times a narrow elongated cell is seen, and the smaller cells are more abnormal in shape than the larger. They sometimes are somewhat oyster-shaped, and at times bizarre-shaped cells occur. Rarely fine stipling and occasionally polychromatophilia is to be seen; and rarely a *true normoblast*. The reticulated red cells are 3.5 per cent.

This evidence of disturbed erythropoiesis in the presence of a high red count and hemoglobin is frequently seen in myelogenous leukemia, and such a picture is, I think, probably never seen in Banti's disease. This red-cell picture with a high red count may occur in other conditions, but relatively rarely in others than polycythemia vera. In this connection it is inter-

esting to note that it has been suggested that polycythemia vera is the red cell homologue of the white cell condition known as myelogenous leukemia. I have seen 2 cases which have shown early in the course of their disease polycythemia, and later died with the pathology of myelogenous leukemia. I have also seen polycythemia vera in a woman whose sister has had classical myelogenous leukemia.

Further observations on the blood of this case before you showed that the *platelets* were definitely increased above their normal numbers, and were not infrequently abnormally large. An unusual number of these small important elements formed from the giant cells—megakaryocytes—of the bone-marrow is the rule in myelogenous leukemia. In certain instances they may be temporarily decreased. Sometimes I have seen in myelogenous leukemia, associated with a greatly increased number of platelets, true megakaryocytes in the peripheral blood.

From what has been said about the blood of this case, taken together with the fact that the patient has an enlarged spleen, the diagnosis of *myelogenous leukemia* is established. It is, of course, of an unusual type because there is no great elevation of the white count. Cases of this sort may occur with white counts under 9000; and in such cases careful blood examination, in contrast to routine examination, may alone be the method of differentiating the condition from Banti's disease. Some cases of myelogenous leukemia may run the whole course of their disease with relatively low white counts, while others may spontaneously exhibit at one time a low count and at other times a high count.

The fact that the blood condition was not recognized in this case (III) by the house officers doing the routine laboratory work is not because of their lack of care or knowledge, but because the condition is difficult to recognize. It may be only because of the clinical picture that we shall be led to study the blood unusually critically, and thus establish the diagnosis in such instances. This form of mistake, dependent upon true difficulty in judging correctly what one sees under a microscope, is of a much more pardonable nature than the mistake illustrated

in the last case (II), where the presence of a large spleen was apparently ignored and peptic ulcer was diagnosed instead of Banti's disease.

This case (Case III) should be given treatment by exposures to radium or the Roentgen rays. The possibility of splenectomy in such cases has been referred to when we discussed the use of splenectomy in general.

CASE IV

This fourth case with a large spleen is perfectly simple to diagnose, and I shall have time simply to comment on some of the symptoms and the treatment.

The patient is a woman thirty-five years of age, whose history is entirely unimportant except for the following: Eight months ago she began to feel tired, lazy and sleepy constantly, and has continued to feel this way ever since; she feels more so now than some months ago. The patient has lost 20 pounds in weight during this time, and now weighs 160 pounds. In the past six months she has had a poor appetite, and has had some mild epigastric discomfort, and a slight full feeling in the left side of her abdomen. Though an intelligent patient, she has not noticed any mass in her abdomen. In the past two months cramps have occurred at times in the calves of her legs. She never had these before. About three weeks ago she began having, and has had every few days since, sharp momentary darting pains running down both legs, particularly the left one.

The *physical examination* is essentially negative except for a large spleen that reaches the umbilicus and fills the greater part of the left upper quadrant of the abdomen.

The *laboratory examinations* are all negative except for the *blood,* which shows as follows:

Hemoglobin, 75 per cent. Red count, 4,900,000.

The *red cells* show slight achromia and a definite variation in size, with an occasional microcyte, but no real macrocytes. Variation in shape is slight. Polychromatophilia occasionally occurs, and rarely stipling. Rarely a normoblast is found.

The *white count is 300,000.* The differential count is:

Polynuclear neutrophils	42	per cent.
Polynuclear eosinophils	3	"
Polynuclear basophils	1	"
Myelocytes: neutrophils	35	"
Myelocytes: eosinophils	3	"
Myelocytes: basophils	1	"
Large mononuclear cells	3	"
Lymphocytes	12	"

The platelets are definitely somewhat increased in numbers.

The blood-picture gives us at once the diagnosis, namely, *typical chronic myelogenous leukemia.*

The *symptoms* this patient presents are the typical ones given in cases of this disease. It is a feature of the disease for the patients to give for their first symptoms weakness, fatigue, sleepiness, or feeling "dopey," or for these symptoms to be among their first symptoms. Such symptoms, you will recall, were a feature of Case III, as they are of this case (Case IV). Loss of weight is also a common feature, and this, combined with symptoms of fatigue, etc., should always make one consider the possibility of this disease. Though most cases present these two features, all do not.

Some cases first consult a doctor because of the enlarged spleen *per se*, or because of discomfort dependent upon the enlarged organ. Probably many cases do not consult a doctor for months after the disease has started because the onset is very gradual and the disease may progress considerably without the patient having any symptoms.

Such darting pains in the legs as this patient describes are not unusual in myelogenous leukemia. We have observed that such pains occur not only in the legs but also in the arms. They have, however, occurred more commonly in the legs, and are usually described as more intense in the left than in the right one—perhaps because of the enlarged spleen. Cramps in the muscles, as also complained of by this patient, are not unusual in these cases.

This patient should be treated by radium or Roentgen-ray therapy. Splenectomy is distinctly contraindicated. She will be referred to the Collis P. Huntington Memorial Hospital of Harvard University for radium treatment, because there is established there a special clinic for the care and treatment of

these cases. With proper radium therapy we can practically assure this patient marked improvement in her symptoms. It is highly probable that her sense of fatigue, sleepiness, etc., will entirely disappear, and that she will gain weight and become symptomless and feel well. The spleen, in all probability, will become much smaller, and the white count will be brought down to somewhere near normal figures; the percentage of myelocytes will fall, and the detailed blood-picture as a whole will appear much more normal, including a lessening of her anemia.

However, though this treatment will produce this effect in the vast majority of cases, particularly if treated relatively early, it does not cure the disease. To keep these patients in the best possible health it is necessary to keep them under close observation, seeing them every few weeks, and giving suitable amounts of radium from time to time. As the disease progresses a relapse occurs, and finally therapy is without significant effect, and the patient dies of the disease. This method of treatment does, however, frequently bring about a temporary remission of the disease, so that patients who are often in a distressing and sometimes in an apparently serious condition can be returned to a useful and functionally efficient existence for a period of many months to some years. Some degree of remission is brought about in practically every case.

The rare acute cases do not benefit by this form of treatment or practically by any other form of therapy. Cases of lymphatic leukemia are not benefited by radium treatments to the degree that the chronic myelogenous cases are. Not infrequently the lymphatic cases receive no particular benefit.

The cases of myelogenous leukemia that have the greatest symptomatic improvement following radium are those in which not only is the white count reduced but also the spleen much reduced in size. Cases in which the spleen is relatively slightly reduced, though the white count may be considerably or even markedly reduced, have, as a rule, a less satisfactory remission.

Through the character of the cells we can usually judge how the patient is doing—whether the process is progressing slowly or rapidly, or whether a stage of terminal chronicity is approaching or occurring, from which there will be no remission.

Though the white count perhaps is the best single guide to further treatment, as time passes by the character of the blood-picture, as well as the presence or absence of symptoms, is certainly equally and perhaps more important. For instance, if the white count has been reduced to well below 50,000, and then rises to this level with the patient feeling perfectly well, and the blood-picture shows essentially no abortive types of cells, and there is a low percentage of myelocytes, and especially if the spleen is small, it is probably fully as wise not to give more radium at this time as to give it. It is, of course, desirable that the patient be observed frequently under such conditions. It is advisable not to give more radium under such circumstances, because it seems as if too many constant exposures may cause in themselves undesirable features, while it is well known that distinctly too much radium may result in a fatal aplasia of the marrow.

If, on the contrary, the white count is 50,000 and the white cells exhibit certain abortive features—in which instance the patient would also probably be having symptoms—more radium may be given. Should such circumstances occur and the patient's spleen be relatively small rather than relatively large, the benefit will probably be slight.

The cases finally progress to a stage with increasing anemia where the blood-picture is of a distinctly abortive type, yet with the white count frequently under 80,000, and the spleen often not especially large. Under such conditions radium often fails to do what it has previously done for the patient; so the individual gradually fails and dies. Thus it is important to give the optimum amount of radium, and to treat the patient and not the white count. One always has to be guided between the amount of good that can be done and the amount of possible harm that may be done.

There are numerous points that I have not mentioned to you that could be profitably discussed about Banti's disease—its differential diagnosis, splenectomy, and myelogenous leukemia—but I have attempted in this hour simply to demonstrate to you certain significant facts about these conditions as illustrated by these 4 cases.

CONTRIBUTION BY DR. JOHN B. HAWES, 2d

Massachusetts General Hospital

TUBERCULOSIS AND INFLUENZA

Necessity of a Sane Conclusion in Reference to the Incidence of Pulmonary Tuberculosis as a Sequel to the Late Epidemic of Influenza

There is prevalent throughout this country, both in the minds of the medical profession as well as the laity, a strong feeling that there is to be a great increase in the incidence of pulmonary tuberculosis as a sequel to the late epidemic of influenza. Boards of health and tuberculosis societies and other organizations are sending out bulletins warning the public in regard to this, while in certain localities the medical profession seems to be somewhat stampeded by this idea. It is of very great practical importance to come to some sane, even if not very definite, conclusion on this subject. Unfortunately, it is impossible to obtain as yet any exact facts and figures, and it will be only after at least a year has passed that we can have any real knowledge on the subject. It will then be too late to undo a certain amount of harm that is now already being done.

The average physician seems to feel that because influenza has been primarily a disease of the respiratory organs, it must on this account have a disastrous effect on a hitherto existing pathologic process in the lungs, tuberculous or otherwise. I admit that this is a perfectly natural deduction, but I do not feel that it is necessarily in accordance with the facts. I was firmly convinced that this would be the case myself, and expected to have many of my patients with quiescent and inactive pulmonary tuberculosis report to me that their disease had broken out into activity once more. I have been agreeably surprised,

on the whole, in finding that this has not been the case. I have seen many patients who have had tuberculosis and who lately have had influenza, more or less severe, who complained of an irritating cough, loss of weight, lassitude, often some fever, and often signs of moisture in the lungs. These patients have been greatly alarmed and much discouraged over what they believed to be renewed activity of their old tuberculous lesion. While I have invariably treated them as if this were the case, I have been impressed and much pleased that in the majority of cases the signs and symptoms soon disappeared. I am not at all sure but I have seen about as many patients complaining of these postinfluenza symptoms—cough, loss of weight and strength, often a slight fever, moisture in the lungs—who have never had tuberculosis and who did not have tuberculosis at the time, as I have those who have had healed or quiescent tuberculous processes.

In the Massachusetts State Sanatoria, out of 1079 patients, there was an incidence of 11.2 per cent. of cases of influenza, and a mortality rate of 1.1 per cent. With one exception our superintendents feel that influenza, even accompanied by pneumonia, seems to have done remarkably little permanent harm to the tuberculous process that already existed. Physicians at Saranac Lake, with whom I have recently talked on this subject, seem to have the same opinion. Not only was the incidence of tuberculosis rather low, but the permanent harm it seemed to do was comparatively slight. One would naturally explain this by taking it for granted that the patient, having developed a certain amount of immunity to tuberculosis, had also acquired some immunity at least against this other respiratory disease—influenza.

It is interesting to compare the comparatively low incidence of influenza among the tuberculous patients at our state sanatoria with that among a similar group of patients in other institutions where there was comparatively little or no pulmonary tuberculosis. Among 4855 such patients, inmates of five state institutions, there was an influenza incidence rate of 30 per cent. and a death-rate of 2.1 per cent., while at one large general

hospital where there were 175 nurses at the height of the epidemic in October, 48 per cent. of these came down with influenza. These figures certainly show fairly conclusively that influenza was less frequent and did less harm, as far as death was concerned, among consumptives than it did among others not suffering from this disease.

Dr. Donald B. Armstrong, director of the Framingham Community Health and Tuberculosis Demonstration, in a recent article entitled "Does Good Health Pay?" calls attention, in a little different way, to this same fact. In his investigations at Framingham he has noted that influenza seemed to have been distinctly more severe, and the mortality seemed to have been greater among those robust and strong individuals who have always enjoyed good health, while among those who have been weak, physically below par, whether suffering from tuberculosis or not, the disease has been milder and the toxins less virulent.

The diagnosis of tuberculosis, difficult at best, is certainly made increasingly so at the present time. Patient after patient has come to me, accompanied by distracted parents, relatives, or friends, who has been told that he has tuberculosis. Upon investigation, I have found many of these patients were merely suffering from the after-effects of influenza, and that there was not sufficient evidence upon which to base a diagnosis of pulmonary tuberculosis. The treatment, except that I did not send them to a sanatorium for consumptives, has been the same as if they had tuberculosis. The "Diagnostic Standards in Pulmonary Tuberculosis," prepared for the benefit of the Framingham Demonstration, and now widely used throughout the country, have, I believe, been of distinct value in clarifying our ideas on the diagnosis of this disease. Unfortunately, at the present time, even these standards, conservative and sane as I believe them to be, must be modified somewhat to suit present conditions. Dr. Arthur K. Stone recently told me, for instance, that, in his opinion, the man who made a definite diagnosis of pulmonary tuberculosis in the absence of a positive sputum or a definite history of tuberculosis prior to this epidemic was taking

a somewhat rash step, and was liable to do harm rather than good. With this opinion I am in hearty accord.

In my work among lung cases at the Massachusetts General Hospital, as well as in my own private practice, I have had constantly to unmake diagnoses of tuberculosis, based on what I believe to have been insufficient evidence. I frequently write on the patient's record, after a definite diagnosis of pulmonary tuberculosis had been made by some other physician, a note to the effect that "I do not believe there is sufficient evidence to make a positive diagnosis in this case," that "I do not believe he should be sent to a sanatorium, but that he should be kept under observation until the diagnosis is made clear, one way or the other." I am glad to state that in many instances I have seen the pulmonary signs clear up, and the patient's general condition return to normal in the course of a few weeks of careful observation and proper hygiene. Of course, no one can say, in such cases as this, that tuberculosis was not the cause of the patient's signs and symptoms, but, on the other hand, no one can say so soon after such an epidemic as this that a given patient's signs and symptoms were due to tuberculosis, and not merely after-results of influenza.

Therefore, until the contrary is proved, I do not think that it is wise to spread the report broadcast that there is sure to be a great increase in tuberculosis. While we certainly should be on the lookout for such cases, and should make repeated sputum examinations and keep all doubtful cases under observation, it is not fair to the individual patient nor to the public to take it for granted that signs and symptoms which under ordinary circumstances we would attribute to tuberculosis, and rightly so, are at present necessarily due to this disease.

The following cases emphasize certain points in this discussion, and show the need of conservatism and extreme care before making a definite diagnosis of pulmonary tuberculosis under present conditions:

Case I.—G. F. A strong, healthy woman of twenty-four came to see me in January, 1919, with the following history: Her mother died of tuberculous peritonitis, and in one brother

there was some question as to his having had pulmonary tuberculosis. In December, 1918, while serving as a pupil nurse in a large hospital, she was suddenly taken with a pain in the left side of her chest. This gradually increased until she was obliged to go to bed. Two weeks later 500 c.c. of clear fluid were aspirated. She ran a temperature of over 100° F. while in bed, and runs a slight afternoon fever at present. The fluid has gradually decreased until at the present time there is practically none. Her general condition has steadily improved. According to the last *x*-ray and clinical examination there is no involvement of the lung itself nor any signs of fluid.

Here is a frank pleurisy with effusion, coming on suddenly in a remarkably strong and healthy woman, with, however, some tuberculosis in her family. According to the diagnostic standards mentioned above, "one should consider a typical pleurisy with effusion as presumptive evidence of tuberculosis." The question at once arises in this instance, whether or not this patient should be definitely stamped as having pulmonary tuberculosis. Personally, I should say no to this question. The treatment has been identically the same as if I believed it to be tuberculosis, and, I am free to admit, in dealing with a patient with as high degree of intelligence as in the present instance, it is a matter of almost academic interest alone as to whether or not we use the word "tuberculosis." Under other circumstances, however, one can easily imagine that it might be a tremendous blow to the patient and to the family to state definitely that this was tuberculosis, even if only in the mild form that these pleurisies usually take. Every physician who has been thrown at all intimately with influenza patients during this present epidemic has seen cases of pleurisy with effusion develop and quiet down, where the evidence was strong that it was the so-called "influenza organisms" (usually a strain of pneumococcus) and not tuberculosis that caused the pleurisy. I have not reported this case as tuberculosis, and I have told the patient and her family frankly that I do not believe that it is tuberculosis.

Case II.—M. B. This man, a strong and healthy appear-

ing Jew, aged thirty, came to see me in December, stating that two months previous he had had influenza for two weeks. Shortly after this he spat up some blood—not as much as a teaspoonful in all. His sputum was examined by a local board of health, where it was reported to be positive. When I first saw him, aside from the fact that he had raised this blood, which was hardly enough to dignify with the name of a hemorrhage, and was said to have a positive sputum, he felt perfectly well. He had a normal temperature and pulse, and his general condition was excellent in every way. His throat was red and streaked with mucus. In the lungs I could hear absolutely nothing except an occasional dry râle. I told him that with a positive sputum he must, of course, consider himself as having tuberculosis, and must take the greatest care not to infect others. As he appeared to me to be perfectly well I allowed him to continue at his work. Two months later I saw him again. He was greatly disturbed because on account of a slight pain in his chest he had recently gone to a large public dispensary and was told that he must go to a sanatorium at once. Again his temperature and pulse were normal, his general condition excellent in every way, and he had gained 10 pounds in weight. This time, over the lower half of the left chest I found numerous sticky râles, but no evidence of consolidation or changes in the voice or breath sounds. I wrote on his record that this was not clinical tuberculosis. A month and a half later I saw him again, and could find only an occasional dry râle, and at my last examination I could find nothing wrong with his lungs whatsoever. I have examined his sputum myself and found it negative.

With a positive sputum, this case must be considered one of tuberculosis, although my own sputum examination has failed to reveal any trace of this disease. In his lungs I have at no time found anything that would even suggest tuberculosis, while from a general point of view he has been perfectly well. I insisted that he change his occupation—a baker—to something else where he would be of no danger to others, which he did. I am unwilling to call this a case of tuberculosis, and have told him that I do not think that any of his symptoms justify

this term. He is to keep under my observation at regular intervals in the future, and I believe understands the situation clearly.

CASE III.—J. R. O'N. This patient, a young man of twenty-five, was accepted as a student pilot in the aëroplane service in December, 1917. He caught cold in April, 1918, and was sent to an army hospital for thirteen weeks, where a definite diagnosis of tuberculosis was made. While there, he had a fever up to 102° F., with, however, a low pulse. Sputum examinations were constantly negative. He gave a history of having been sent away for a couple of months six years ago on account of his health, although no definite diagnosis was made. My examination in October, 1918, showed a normal temperature and rather rapid pulse, weight up to normal, and a right apex with slight dulness and signs of slight old fibroid tuberculous process. The lower half of the left chest in the back was dull, with diminished voice and breath sounds, signs of small amount of fluid and a thickened pleura. I told him that he should report once a month, and allowed him to continue his work. This he has done regularly. In January he had a mild attack of influenza and stayed at home a few days. Since then he has improved steadily; all that I can now find in his lungs are a few dry râles at the right base, where the influenza was localized. He is working every day.

Here is a man with an old quiescent tuberculosis, sufficient to cause his discharge from the army. He undergoes a mild attack of influenza, apparently without its causing any increased activity in his tuberculous process. Nevertheless, it would be very easy for anyone seeing this patient for the first time shortly after his influenza in January to have said that this was a case of tuberculosis roused into activity by influenza. I really do not feel that this has happened, nor do I feel that the influenza has done his tuberculous process any harm whatsoever.

CASE IV.—R. McN. This patient, a young man of twenty-one, came to see me March 1, 1919. His mother was said to have died of tuberculosis. He himself has always been strong and robust. In Christmas, 1918, he was taken with the influenza

and was in bed nine days. He went to work as a chauffeur shortly afterward, but about ten days ago had a hemorrhage of about an ounce of clear blood, followed in the course of the next twenty-four hours by the raising of a large amount of foul pus. At present he feels perfectly well and has no symptoms. Physical examination shows little, except slight dulness at the bases. *x*-Ray examination shows mottling over both upper lobes. Later examinations have shown absolutely no signs of activity in the lungs, while the patient himself feels perfectly well and is working regularly.

In this case there was apparently a slight tuberculous infection at the apices, as shown by the *x*-ray. The patient had never known of this, however, nor has it ever caused him any symptoms. After his influenza there was apparently a patch of what must have been an unresolved pneumonia, which broke down and was accompanied by the raising of blood, followed by pus. According to the diagnostic standards, "a hemorrhage of at least a teaspoonful of bright blood is presumptive evidence of pulmonary tuberculosis." Under ordinary circumstances, one would be justified in saying that this was probably pulmonary tuberculosis. Under present conditions, however, I do not feel that this is the case, nor do I feel that the influenza has had any effect on his quiescent tuberculosis.

CASE V.—F. S. This patient, a woman of thirty-one, had always been delicate, especially during the past five years. In January, 1919, she had a mild attack of influenza, and has had a cough ever since. Sputum has recently been found positive by a local board of health. Physical examination shows a woman in a marked state of what I believe to be postinfluenzal depression, with a subnormal temperature, low blood-pressure, rather rapid pulse, and some anemia. I could find absolutely nothing wrong in the lungs, despite the positive sputum. I have advised her to put herself at as nearly absolute rest as possible, and to let me see her in a month's time.

Here again we have a case with positive sputum on one examination. The symptoms, however, are far more those of the physical depression so characteristic of the recent epidemic

of influenza, rather than those of any active tuberculosis. This is confirmed by the fact that the signs in the lungs were conspicuous by their absence. Are we going to say that this woman has tuberculosis as a result of influenza, or are we going to take the more conservative course, and treat her as if she had tuberculosis, keep her under observation, and yet not add to her depression by using the term "consumption." To some this latter may seem a form of camouflaging the truth; to me it seems the only humane course to pursue.

Case VI.—J. G. A physician in charge of the tuberculosis dispensary in another Massachusetts city made application for this man's admission to one of our state sanatoria. After looking over the application blank, I was in some doubt as to the diagnosis, and wrote to the doctor as follows: "I note that the signs are entirely at the bases of the lungs; likewise that there is a negative sputum, a normal temperature, and a fairly normal pulse. You state that this condition is a sequel of influenza. I would like to know on what you base your diagnosis of tuberculosis in this instance? There are so many cases where the signs are located at the bases of the lungs following this influenza which are called tuberculosis, but which really are simply the sequel to influenza and due to the same organisms which caused the influenza, that I am trying to weed out all doubtful ones." I received his reply to the effect that he considered this patient to have a general influenza bronchitis, but the fact that it persisted and that the man was not doing well made him fear that he might be doing this patient an injustice by not sending him to a sanatorium. I wrote at once, stating that I would gladly give this man a trial at the Rutland Sanatorium, hoping thereby not only to improve his general condition, but to clear up the diagnosis.

Were I not to follow up this particular case after his admission to the sanatorium to find out whether or not this was tuberculosis, this man would go down automatically on our list as a case of consumption following influenza. While in this instance it certainly will do no harm to send him to a sanatorium for consumptives, and will probably do him much good, I feel

that this course should be pursued only in exceptional instances.

Cases similar to these might be endlessly multiplied. I do not wish to give the impression that I believe influenza is not an extremely dangerous respiratory tract disease, and that it does not do a certain amount of harm in practically every case. On the other hand, I wish to go on record as being definitely of the opinion that not only do patients who have or who have had pulmonary tuberculosis possess a certain degree of immunity or resistance against influenza, but that in my experience, at least, influenza or influenza-pneumonia does not seem to have done the great harm to the already diseased lung that most of us, myself included, thought would be the case.

As I have stated before, I have seen and am seeing many patients whose old tuberculous processes have *apparently* been lighted up by an attack of influenza. I am constantly receiving applications from physicians all over Massachusetts for the admission of patients to our state sanatoria whose disease, according to the statement on the application blanks, has been lighted up and rendered active by influenza. My experience so far at least, and I admit that it is too soon to speak definitely on this subject, has been that in the case of many of these patients the extensive signs in the lungs following the influenza have rapidly cleared up, leaving the old tuberculous focus comparatively little worse than it was before.

A physician in New Hampshire recently told me that he was making routine examinations of all his influenza patients one or two months after the acute symptoms of the influenza had subsided. I believe that this is an excellent course to pursue. I believe that all doubtful cases should be sent to a sanatorium or other similar institution for study and observation. I do not believe, however, that we should take it for granted, as is being done in many instances, that signs in the lungs and constitutional signs and symptoms persisting long after an attack of influenza are necessarily due to tuberculosis.

CLINIC OF DR. FREDERICK T. LORD

Massachusetts General Hospital

A PULMONARY DESTRUCTIVE LESION

A Case Teaching Exercise,[1] with Remarks on History-taking, Physical and Certain Special Examinations in Diseases of the Lungs, and the Diagnosis and Treatment of Pulmonary Abscess.

The following case history represents an actual and urgent problem and may well serve the double purpose of material for an exercise in case teaching and the placing on record of an instructive pulmonary lesion. In the criticism of this or any record it should be the purpose in reviewing it to note what of consequence may be lacking and how the work might have been better done.

You are asked in your report[2] on the case to state (1) what more you would like to know, (2) the diagnosis, and (3) the treatment you would recommend. You need have no hesitation in expressing yourself freely in criticism of the records. Regarding the diagnosis you make, to speak frankly but without any ungracious intent, I may say that while I am pleased when your diagnosis is right, I take a certain satisfaction in your mistakes, from which I can judge your deficiencies. It is a rare opportunity to make a mistake to your own advantage and not to the detriment of the patient.

The case history for consideration is as follows:

[1] I have used the case history in my Course in Physical Diagnosis and Medical Practice for Graduates at the Massachusetts General Hospital, but the present discussion of the case was put together for the purposes of this article.

[2] The case histories are distributed before the exercise, and each member of the course is asked to hand in a written report.

History.—Miss Y., forty-three, born and living in Massachusetts, consulted me October 6, 1914. The history is reported as if taken today.

Concerning her family history, her mother died of tuberculosis when she was four years old, and she was exposed. Her father died of "creeping paralysis." A half-brother is well.

Of past illnesses, it may be noted that she had a gland in the left side of the neck thirty-three years ago. It did not rupture and was not operated. Over a period of six to seven months twenty-seven years ago she had a cough. She cannot remember whether during this interval she had fever, night-sweats, or loss of weight. She remembers that there was ulceration of both corneæ twenty-six years ago, but she cannot recall whether or not the term "phlyctenular" or "scrofulous conjunctivitis" was used in connection with this disturbance, and she does not know the cause of the ulceration. There is no history of hemoptysis or pleurisy. Following scarlet fever she had abscesses in the left ear. She has had measles. There was a nervous breakdown nineteen years ago lasting one year. Since the age of fifteen she has had hay-fever of the fall type. There is no history of chorea or rheumatism. While in Rome, three years ago, she had a neuralgic pain in the region of the left ear, lasting three days.

There is nothing noteworthy regarding her habits. She is not accustomed to take alcohol. The bowels move regularly each day. The catamenia is regular and lasts three days. The flow is not excessive and there is no pain. The last period was three weeks ago.

Regarding the present illness, she states that nine months ago, without preceding respiratory disturbance, she nearly fainted, and had chill, fever, and weakness. The fever lasted two to three days, 101° F. being the highest temperature. There was no cough, rhinitis, or sore throat at this time. At the end of three days she had severe pain in the left side of the head in the region of the left ear. The pain lasted twelve to fifteen hours out of the twenty-four, and continued for nearly three weeks. A week after the onset of the present illness she had the following:

After having been abed for about an hour and asleep or

dozing, there was a sudden and violent paroxysm of cough without expectoration or noteworthy dyspnea. The paroxysmal cough lasted for one to one and a half hours and during it there was a sensation of bad odor and bad taste in the mouth. She vomited without nausea during the attack. There has since been a recurrence of the paroxysmal cough without expectoration six times each day and slight cough in the intervals between the attacks.

Following this she went away, feeling badly and continuing to cough. During the next seven weeks her temperature was taken at irregular intervals and was found to be elevated for varying periods, once for as long as ten days, the variations in the temperature being from 99° to 100.6° F.

Seven months ago she awoke at 5 A. M. with intense pain in the left axillary region, much aggravated by cough and long breath. The pain lasted one week, and during this time the temperature was elevated, but always below 100° F.

A week after the onset of the pain there was a gush of about an ounce of green, foul-smelling pus, which came up with the cough, the cough having previously been without expectoration. Cough and expectoration have persisted since and evening elevation of temperatute from 99.2° to 99.4° F. continued until about six months ago, when she went to Georgia, where she continued to cough and expectorate, but was without fever.

About five months ago she had a second attack of pain, this time on the right side, lasting about two weeks.

Between three and four months ago for a period of about a month she lost her voice, and for part of the time could not speak above a whisper.

About three months ago the cough was less troublesome and she felt better, but after a walk she had fever and subsequent afternoon elevation of temperature off and on to two months ago, when she had a third attack of pain, this time on the left side, in the region of the scapular line and posterior axilla. The pain lasted for five days and was accompanied by fever. There has since, with the exception of a few days, been an evening elevation of temperature from 99.4° to 100° F., while the morning

record has usually been normal. The sputum averages about 3 ounces in twenty-four hours and is purulent and green in color. She coughs at frequent intervals during the day and raises something every time she coughs. Every few days the amount of sputum is greater, and on these days it usually has a bad odor and taste, while on the intervening days it is likely to be little or not at all offensive. The amount has never exceeded 1 ounce at any one time. About seven months ago the sputum contained a small amount of blood surrounding the purulent masses, and on two occasions since it has been bloody. About three weeks ago the sputum contained about 1 dram of blood, and a few days ago it was stained a brownish color.

The cough is paroxysmal, the attacks recurring at frequent intervals during the day. It is uninfluenced by position. She has been short of breath for seven months. She had night-sweats for about two weeks after each attack of pain. Her average weight is 130 pounds. The weight is now 134 pounds. There is no nausea or vomiting. The appetite is poor.

Physical examination shows a well-developed and nourished woman. The skin and mucous membranes are of good color. The pupils are equal and react to light. Their outline is slightly irregular. There are corneal scars in both eyes. Examination of the right fundus with the ophthalmoscope is negative. The left is not seen on account of the corneal scars. There is no glandular enlargement. The mouth shows many filled teeth, one carious stump in the left upper jaw, and some pyorrhea. There is a slightly musty odor to the breath. There is no tenderness over the sinuses. Examination of the ears with the otoscope is negative. The nasal cavities, the throat, and the nasopharynx show nothing abnormal. Inspection of the larynx with the laryngoscope is negative. As far as can be seen with this instrument, the trachea shows nothing abnormal.

The cardiac impulse is palpable in the fifth space, nipple line, with corresponding dulness 12 cm. from the midsternum. The right and upper borders are normal by percussion. The heart sounds are regular, of good quality, and there are no murmurs. The pulmonic second sound is greater than the aortic second sound, but not abnormally accentuated.

Inspection of the chest shows no asymmetry. Expansion of the left lung is slightly restricted. On palpation, the intercostal spaces are the same both sides. There is no abnormal supracardiac or spinal dulness. The apices of the lungs show nothing abnormal. Pulmonary excursion determined by percussion during full expiration and inspiration is equal and of good amplitude on both sides. In the left back in the paravertebral region, between the seventh space and the tenth rib and over an area extending laterally to the posterior axillary line, are the following signs: There is slight dulness apparently of the same degree throughout the dull area. There is also slightly increased and bronchial breathing, increase of voice (without egophony), increased whisper, and much diminished but not absent tactile fremitus. No râles are heard. There is no cracked-pot sound, amphoric breathing, tympany on percussion, or change in the percussion note on changing the position of the patient.

Examination of the abdomen shows nothing abnormal. The liver, spleen, and kidneys are not made out to be enlarged. The spine is negative. The knee-jerks are present and normal. There is no edema. Blood-pressure is 120 systolic and 80 diastolic.

The blood shows a white count of 10,600, of which 85 per cent. are polynuclear cells and 15 per cent. lymphocytes. Wassermann test on the blood is negative. The urine is normal, acid, 1028. It contains the slightest possible trace of albumin, but no sugar. The sediment shows a few squamous cells, an occasional leukocyte, and no casts.

The sputum amounts to about 3 ounces in twenty-four hours, is green and purulent, with a slightly musty odor. Three specimens are negative for tubercle bacilli. No actinomyces, blastomyces, or streptothrices are seen. There are numerous small organisms morphologically like influenza bacilli, many cocci, and a few bacilli. In one of three specimens there is a small curled, elastic tissue fiber, without alveolar arrangement. No tumor fragments or tumor cells are found. Five previous specimens of sputum are said to have been negative for tubercle bacilli.

x-Ray examination shows some peribronchial thickening and there are numerous small apparently calcified areas, and a small calcified spot at the right apex. In the left lower chest there is a well-circumscribed area beginning above at the eighth and below at the tenth rib, and extending outward to the axillary border, of oval shape, and measuring 4 inches in greatest diam-

Fig. 241.—

eter and 2 inches in width. There is no evidence of a foreign body.

Criticism of the Record.—*The History.*—The most important guiding principle in history-taking is always to try to make a preliminary diagnosis from the history alone. The first matter for consideration is whether the history is as complete as it should be. We are dealing here with a problem in pulmonary diagnosis, and in all such cases the possibility of tuberculosis should be constantly in mind. An inquiry has evidently

been made in this case concerning those features which have a bearing on this question. Then you will note that in the description of the present illness the evolution of the symptoms is given. In pulmonary problems the number of possible symptoms are few, and much importance may be attached to the order of their appearance. Many mistakes in the diagnosis of disease of the lungs as well as of other organs may be ascribed to insufficient attention to the march of events. The relation in point of time of hemoptysis to other symptoms is, for example, an important matter, and in this case it should be noted that there was a small amount of blood surrounding masses of sputum after the cough had lasted for about seven weeks, and frank hemoptysis after about six weeks of cough and expectoration. It is in general true that hemoptysis out of a clear sky, or when cough and scanty expectoration alone cloud it, is almost invariably due to pulmonary tuberculosis. Blood surrounding masses of mucus, however, can hardly be regarded as hemoptysis in the general acceptance of the term. In this case, therefore, the hemoptysis late in the illness is less suggestive of tuberculosis, but hemoptysis out of a cloudy sky is also often due to tuberculosis.

The evolution of symptoms is also of importance in many other pulmonary conditions, and among them pulmonary embolism and infarction, of which there are suggestive features in this case. In fact, the distinction between pulmonary infarction from a latent venous thrombosis and pneumonia can at times only be made by attention to the sequence of the symptoms. In pulmonary infarction pain in the side is the most constant and usually the initial symptom, and if there is a succession of emboli the pain may be first on one and then on the other side, due to embolism of one and then of the other lung. Pleural pain in the first instance on the left and next on the right side is somewhat suggestive of embolism and infarction in this case. When infarction involves an area of considerable size cough and bloody expectoration occur within a few hours to two or three days after the pain, and the temperature slowly rises, while in pneumonia the pain, cough, bloody expectora-

tion, and rapid rise of temperature occur at once or in rapid sequence. Small emboli may give rise only to pleural pain without subsequent cough and bloody expectoration, and in this case if embolism occurred the clot was probably too small to cause typical symptoms, but the record should have been amplified with respect to the events following each attack of pleural pain.

Physical Examination.—Are there omissions in the physical examination? Nothing is said of bronchoscopy. Bronchoscopy is to be considered from the point of view of its danger and the advantage to be derived from its use. Many lives which might be saved are lost each year in consequence of the aspiration of foreign bodies because of the slowness with which medical men have informed themselves of the progress made in the use of the bronchoscope, and it is essential that wide stretches of the country now unprotected be supplied with physicians skilled in its use. But its use is more particularly urgent in the period immediately following the inhalation of a foreign body to prevent the immediate and remote consequences. A bronchial tumor or an aspirated foreign body is to be considered in this case, and bronchoscopy might establish the diagnosis. A tumor could hardly be successfully removed by this means. The removal of a foreign body lodged so long in the bronchi would not be likely to relieve the secondary and chronic inflammatory changes, but might alleviate the symptoms. The bronchoscope is of itself not without danger, and the symptoms do not seem sufficiently suggestive or the prospect of relief hopeful enough to justify its use here.

The use of tuberculin is not mentioned, but the presence of fever may be regarded as a contraindication, since an elevation of temperature is the principal feature of the test.

Inoculation of a guinea-pig with the sputum would be desirable, but we should have to wait six weeks at least for the development of tuberculosis in the animal, and it would seem best to come to some conclusion regarding the problem before this time. This also was not done.

Irregularity in the outline of the pupils when accompanied by inequality and failure to respond to light is suggestive of

syphilis, but only irregularity is present here, and is probably due to a disturbance in the iris at the time the corneal opacities were formed. The pulmonary condition does not suggest syphilis, and it seems quite unnecessary to pursue the investigation further than the negative Wassermann test, which should be done as a routine. If syphilis could be entertained as a possibility then a numerical and differential count of the cells in and tests for protein and Wassermann on the spinal fluid should be done, but the withdrawal of spinal fluid is not a wholly indifferent matter to the patient and there should be some definite indication for its performance.

Regarding examination of the chest, I can perhaps help you by telling you how you can yourself get the most in the way of instruction out of your investigations.

Skill in percussion is usually the last and most difficult acquisition of the student. You should always do your percussion of the chest first. Light seems preferable to heavy percussion. Percussion should be rapidly done so that slight differences are more readily appreciated by an immediate contrast of abnormal with normal resonance. The mere finding of a dull area is not enough. Its limits and the character of the dulness throughout all parts of the region should then be determined, and it is of interest to know that the dulness was of the same degree throughout the dull area here. An error, commonly made in the percussion of dull areas at the lower limits of the lung, is to fail to note the degree of dulness at the extreme base. In the period during which we have controlled our chest findings with the *x*-ray there have been a number of cases in which the *x*-ray has shown an uninvolved portion of the lung between the upper limit of the diaphragm, and the dull area on percussion and reinvestigation has shown that greater care in the determination of the limits of the area by percussion would have disclosed this. Once you have learned the rudiments of physical examination, no one can teach you percussion with an advantage equal to your own in the immediate check on percussion by the use of the stethoscope. In the case under discussion the changes found with the stethoscope immediately confirm the

previous and independent observation of dulness. You should thus let one method serve as a check against the other to make the most of the opportunity.

There is no other recent addition to our methods in pulmonary diagnosis of equal educational value to the *x*-ray. Just as percussion may be checked by the stethoscope, so the final results of physical examination may be confirmed or not by *x*-ray examination, but to realize fully the educational value of the *x*-ray all physical signs must first be recorded. There are, however, limitations to the *x*-ray, and it cannot be expected to demonstrate certain shadows which are below the level of the dome of the diaphragm or behind the shadow of the heart. The *x*-ray findings in pulmonary and other conditions should be regarded only as part of the evidence, and a final conclusion reached only after full consideration of all the data.

A Student: How do you interpret the physical findings in this case?

Dr. Lord: The correlation of physical signs with pathologic lung conditions shows that there are two well-defined groups of signs corresponding to two groups of lesions. Dulness, bronchial breathing, increase of voice, whisper, and tactile fremitus are found when there is increased density of the pulmonary tissue and patent bronchi within the consolidated region, as in ordinary lobar pneumonia, bronchopneumonia, pulmonary infarction or retraction, and compression of the lung. Dulness, diminished or absent breathing, voice, whisper, and tactile fremitus are common to all lesions where there is increased density and lack of communication of the involved region with the bronchi, as with an accumulation of fluid or a tumor in the lung or pleura, cysts, atelectatic areas from bronchostenosis, and massive pneumonia. The signs here do not fall into either group and suggest a combination of a member of one with one of the other group. The dulness, bronchial breathing, increased voice, and whisper suggest a consolidation of the lung with patent bronchi due to pneumonic infiltration or infarction, and the diminished tactile fremitus, in addition, suggests fluid or solid in lung or pleura without free communication with the

bronchi. The absence of râles suggests that pneumonic infiltration if present is relatively inactive and probably of the indurative variety. From the signs alone no further conclusion as to the nature of the process seems justifiable.

Such evidence against cavity as the absence of cracked-pot sound, amphoric breathing, and tympany on percussion are of no value in excluding it. A small cavity or small multiple cavities, if present, would not be likely to show any of these signs. Much depends on the position of the cavity, whether deep or superficial, and the freedom of communication with the bronchi. The smallest cavity detected as such in our series measured at autopsy 3 by 2 cm. and was just under the pleura in the posterior aspect of the left lower lobe.

Is there anything further you would like to know about the sputum?

STUDENT: I should like to know if it separated into three layers on standing.

DR. LORD: Why?

STUDENT: Because it would then have a bearing on the diagnosis of bronchiectasis.

DR. LORD: The sputum from patients with bronchiectasis will often separate into three layers on standing. The separation into layers depends on the admixture of part of the sputum with air and mucus, so that there is an air-holding frothy layer containing mucopurulent masses at the top, a thin cloudy fluid in the middle, and a sediment of pus at the bottom. But this appearance is not peculiar to the sputum with bronchiectasis, and is seen with pulmonary abscess and the evacuation of empyema through the bronchi. I do not think stratification of the sputum is of diagnostic value.

An omission may be noted in the *x*-ray examination. If *x*-ray of the left mastoid showed increased density it would help to explain the history of pain in the ear three years ago, and again at the onset of the present illness, but would not solve the question whether lateral sinus thrombosis and pulmonary embolism were concerned in the lung disturbance. No *x*-ray of the skull was taken in this case.

There is something lacking in the description of the *x*-ray findings. Can anyone suggest what is wrong?

STUDENT: Was the *x*-ray taken with the patient in the upright or the prone position?

DR. LORD: That is an important matter. Why?

STUDENT: Is it not true that *x*-ray plates in such cases should if possible be taken with the patient in the upright position in order not to miss the appearance of a cavity with fluid level?

DR. LORD: Yes, and that is one defect in the report. Is there any other?

STUDENT: I should like to know the character of the area, whether there is in this region mottled uneven density or an unevenly dense shadow and the degree of density.

DR. LORD: This is also an important inquiry. In answer to the first question, the *x*-ray plate was taken with the patient prone and there would then be no evidence of fluid level. The importance of position in the *x*-ray diagnosis of lesions in which there may be losses of pulmonary substance with fluid free to show a fluid level was not fully appreciated at the time this patient was under investigation. If air and fluid are present in a pulmonary cavity, the central bright area due to the air may be entirely obliterated in *x*-ray plates taken in the prone position, on account of the diminished radiance of the fluid through which all the rays which enter the cavity must then pass.

In answer to the second question, there was an even density of marked degree over the circumscribed area as shown in the photograph. It is important to note this because by making the distinction between mottled, uneven, and evenly dense shadows evidence may be obtained concerning the nature of the process. Mottling suggests a varying degree of infiltration such as may occur in bronchopneumonia. An even density of considerable degree suggests a circumscribed collection of fluid or solid, but it is usually unsafe to make a diagnosis of the nature of the process from the *x*-ray alone.

Still another omission in the description of the *x*-ray findings is the failure to note the amplitude of the diaphragmatic excursion during inspiration as seen with the fluoroscope. It would

be of interest to know this to confirm the finding on physical examination of a normal respiratory motion of the pulmonary margins, and to furnish additional evidence regarding the condition of the left pleura—whether adherent or free.

Etiology.—We have to consider as a cause pulmonary tuberculosis, bronchial or pulmonary tumor, aspirated foreign body, and pulmonary infarction.

The possibility of tuberculosis is suggested by the disease in the family and the opportunity for contagion. The glandular swelling in the neck many years ago and the corneal ulceration, possibly of a phlyctenular type, may be of significance in this connection. There is nothing specially suggestive of tuberculosis in the history of the present illness other than that any pulmonary disturbance calls for its exclusion. The lack of apical involvement on physical and *x*-ray examination is against it, but there are occasional instances of tuberculosis involving the hilus region, and no certain conclusions can be drawn from the site alone. The failure to find tubercle bacilli in specimens of sputum containing elastic tissue is of great importance and goes far toward excluding tuberculosis. We should expect to find tubercle bacilli with pulmonary destruction of such a degree as to give rise to elastic tissue if tuberculosis were the cause.

Bronchial or pulmonary tumor would explain the bloody sputum. The hilus region is a favorite site for neoplasm. Partial occlusion of the bronchus leading to the involved region, consequent stagnation of bronchial secretion behind the obstruction, secondary infection, with bronchiectasis, single or multiple pulmonary abscesses, and interstitial pneumonia would account for the entire picture and cannot be excluded. Tumor fragments and tumor cells were not found in the sputum, but are usually missed when tumor is present. The absence of metastases in accessible regions is not against tumor, but after a duration of nine months one might expect neighborhood involvement and evidence of this in the *x*-ray examination of the mediastinum, or in radial projections from the involved pulmonary region along the course of the larger bronchi. Bronchoscopy would help in the diagnosis. The duration is too long for a malignant growth,

as most cases are fatal within a year of the onset of symptoms, and after nine months this patient is still in good general condition.

An aspirated foreign body can neither be affirmed nor denied, but the aspiration does not usually take place insidiously in adults, though it may occur during sleep. The initial symptoms are paroxysmal cough, dyspnea, a sense of suffocation and cyanosis, followed after an interval of a few days by the secondary manifestations of pulmonary infection. In this case the symptoms of infection—chill and fever—came first and the cough later. The *x*-ray showed no foreign body, but certain foreign bodies are not opaque to the *x*-ray. Bronchoscopy would help in the diagnosis.

Pulmonary embolism must be considered. There is a history of abscesses in the left ear after scarlet fever. Three years ago there was pain in the left ear for three days. Early in the course of the present illness there was again pain in the region of the left ear as a prominent symptom. A latent thrombosis of the left lateral sinus from which septic material separated and found lodgment in the lung as an embolus would adequately account for the pulmonary symptoms. This explanation finds some support in the second attack of pleural pain which occurred five months ago. While the first attack of pleural pain seven months ago and the third attack two months ago may be attributed to extension of inflammation from the left lung to the corresponding pleura, and the right-sided pleural pain may also be due to pulmonary infection proceeding from the lung itself, yet invasion from without, as from a venous thrombosis, is a more likely explanation. Ophthalmoscopic inspection of the veins of the fundus is desirable where thrombosis of the lateral sinus is suspected, since thrombosis of the lateral may lead to interference with the flow of blood in the cavernous sinus and engorgement of the ophthalmic veins. Unfortunately, the corneal scars prevented the examination of the fundus of the left eye. *x*-Ray examination of the left mastoid is also desirable, but was not done in this case.

Diagnosis.—Bronchiectasis is a possibility. It is an unusual

condition and may be suspected in the presence of any chronic pulmonary infection, but is incapable of clinical proof. To raise bronchiectasis often to the position of an independent disease is to fail to appreciate the pathology of the condition. Aside from its occurrence in the rare cases of bronchial asthma without secondary infection it is never found at autopsy unassociated with pulmonary changes of much greater importance than the bronchiectasis itself. Chronic infection of the bronchi is not likely long to exist without extension to the neighboring pulmonary tissue, and a more accurate term is then a "chronic bronchopulmonary infection."

Although the cause cannot be determined, the data point to pulmonary abscess, the five cardinal signs of which may be enumerated as follows:

1. Foul sputum and foul breath.
2. Cough and explosive expectoration.
3. Elastic tissue with alveolar arrangement in the sputum.
4. Dulness on percussion over a circumscribed area.
5. The demonstration by *x*-ray examination of a cavity with fluid level.

The five cardinal signs are not wholly fulfilled. To be certain of a pulmonary origin of the elastic tissue an alveolar arrangement must be demonstrated, and this was not present in this case. Elastic tissue without an alveolar arrangement may come from the pleura or the bronchi as well as the lung. The *x*-ray description does not indicate a cavity with fluid level. It is essential that the plates be taken in the upright position to demonstrate fluid level and, as already explained, the *x*-ray was taken in the prone position in this case. Even in the upright position fluid level would not be shown unless there were both air and fluid in the cavity, and cavities unruptured or completely full of pus would show no fluid level. The necessary conditions seem sufficiently fulfilled, however, to make the diagnosis of abscess amply justifiable. It would seem indeed that less evidence than we have would do, and we often have to be satisfied with less than the five cardinal signs.

The diagnosis would not be complete without an attempt to

go further and define the pathology of the condition. The long duration of the suppurative process suggests that pulmonary induration is likely to have taken place about the site of the destructive process. Even though the area is circumscribed and evenly dense by *x*-ray examination, there may be multiple pockets within the site of involvement. The even density of the *x*-ray shadow, however, is more suggestive of a single abscess. It is important to know whether the pleura is free or adherent over the site of the abscess. Invasion of the pleura is suggested by the history of pleural pain, but the normal amplitude of the pulmonary excursion makes it improbable that obliteration of the pleural sac has taken place.

Prognosis.—What is the probable outcome of this case? The theoretic mortality in pulmonary abscess is 74 per cent. Of the cases which do not terminate fatally, 18 per cent. continue to cough and expectorate, and are constantly subject to the danger of local or general septic complications with their menace to life. In the remaining 7 per cent. complete spontaneous recovery may occur. The small group in which spontaneous recovery may occur, however, comprises only mild and uncomplicated cases of short duration. I have never seen a patient with a history of nine months' duration completely recover from abscess spontaneously. In this case, therefore, there is, so far as I can estimate, great danger to life, an almost certain prospect of continued invalidism, and practically no chance of complete recovery.

Treatment.—There is no satisfactory medical treatment. Quinke's position may be tried, but has not proved successful in my experience. There is but one promising method, and that a resort to operation. What are the dangers? It is a difficult and dangerous operation. It should be undertaken only by one skilled in its use, and even then the results are far from satisfactory in many cases. The operative mortality is high and may be placed at 6 deaths (9 per cent.) in 62 operated cases. Including cases in which the abscesses cannot be found, surgical failure may be estimated at 14 per cent. Surgical success is more likely in the acute than in the chronic cases. The delay

in seeking operative relief in this case has somewhat increased the chief danger of the operation—that of fatal postoperative hemorrhage due to the injury of granulation tissue in the wall of the abscess or of blood-vessels lining the wall or traversing the lumen of the cavity. Delay has also diminished the chance of complete cure because the firmer the pulmonary induration about the abscess, the less likely is the cavity to close after the establishment of drainage. Multiple pockets arising in the course of time by extension into neighboring tissue may make surgical drainage impossible. Bronchiectatic dilatation of bronchi communicating with the cavity may add to the surgical difficulty. Then there are the dangers of postoperative pneumothorax and empyema. The probable lack of pleural adhesions of sufficient density to withstand the operative manipulation increases the operative risk and makes it desirable that an operation, if performed, be done in two stages.

What are the chances with operation? Complete and permanent cure of abscess by operation may, in general, be estimated from our experience at 10 in 62 cases, or 16 per cent. Complete or partial success may be calculated at 38 per cent. In view of the absence of any obvious present complication and the sharply circumscribed and even density of the abscess by *x*-ray examination, and in spite of the long previous duration, the present situation seems as favorable as the general average. If not complete, then partial success may be hoped for in this case. What shall we advise this patient to do? There can be but one answer, and that is to take the risk of operation for the sake of complete or partial relief.

Operation.—Operation (Dr. C. L. Scudder) in first (October 17, 1914) and second (October 24, 1914) stages evacuated about 1 ounce of foul pus from a pulmonary cavity with indurated walls in the left lower lobe 2 or 3 cm. from the surface of the lung. A left pneumothorax developed after operation. Following this the cough and sputum became much less troublesome and the foul odor to the sputum disappeared, but a sinus with a slightly foul discharge persisted. The temperature became normal. A third operation in November, 1915, and a fourth

in May, 1916, were performed. At the last operation the pulmonary cavity was found to be about the size of the end of the middle finger. It communicated with two dilated bronchi, the size of a slate-and lead-pencil respectively. The cavity was cureted. The dilated bronchi were dissected free and tied off. The patient has since been well and without cough or expectoration.

Comment.—The diagnosis was correct in that the patient had a pulmonary abscess. The two dilated bronchi were not diagnosed and could not have been diagnosed. The etiology of the abscess is not known, but septic emboli from thrombosis of the left lateral sinus seem the most likely explanation. The operation was finally a complete success. The localization of the abscess was accomplished without difficulty in this case. Difficulty in sufficiently accurate localization of abscesses for successful surgical approach has hitherto been a troublesome matter, which an improved, portable, *x*-ray apparatus, enabling the surgeon to guide his search by means of the fluoroscopic screen, may obviate. The danger of postoperative pneumothorax, constantly present in operations on the lung through the unadherent pleura, is somewhat diminished by the use of one of the positive pressure methods of anesthesia, more commonly employed now than then.

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THE RELATION OF THE CLINICIAN TO INDUSTRIAL MEDICINE

IN a recent lecture at the Harvard Medical School Dr. Harry E. Mock outlined the growth of industrial medicine and pointed out the economic value to the community from the development of the industrial physician, who is becoming at present a highly specialized man. Up till recent times industrial medicine was confined to the work of the factory surgeon, who administered first aid in case of accidents. Very soon some physicians who entered this field of work recognized the great possibility of service that could be rendered to the employees, employers, and the community. The work of the industrial surgeon, in many industrial plants in this country, has very rapidly grown, and from the mere first-aid treatment the work has spread into many ramifications, such as the physical examination of applicants for employment, to determine the suitability of the particular individual for the particular job, thus rejecting the unfit before they start; the routine examination and treatment of those already employed; the supervision of the sanitary conditions of the plant, and many other lines, all calculated to promote the health of those employed, increasing the industrial efficiency, diminishing labor turn-over, which is a great drain on industry, and preventing the particular establishment from bearing the burden of those physically unfit.

To meet this ever greater demand for such health supervision in industry the position of industrial physician is rapidly developing into a specialty with a wide and most useful field of service. For in the present world crisis all movements tending

to the conservation of human life and safeguarding of human efficiency are of enormous importance.

But the study of the relation of industry to health, the recognition of the effects of industrial hazards upon the health of those exposed to them, is not a field for the industrial physician alone, in fact, it is not even primarily his field.

This field of study, the estimation of the part the patient's occupation had on the development of the disease for which he presents himself for treatment, is a field primarily for the physician who has to diagnose diseased conditions and treat patients in the hospital or in private practice.

Not only is the effect of occupation on health a matter of importance for the physicians in the diagnosis and treatment of the individual case, but inasmuch as occupational diseases are, in a large measure at least, preventable, the physician has certain duties to the community in the control of occupational diseases.

His duties and responsibilities in the control of occupational diseases are not in any way different from his duties and responsibilities in the control of communicable diseases. In this group of diseases also he should be the vanguard of the public health authorities, who, acting on his prompt diagnosis and report of cases, may take the proper measures to prevent the occurrence of other cases.

It is to the importance for the general medical man of recognizing the effects of occupation on health that I wish to direct attention. This field so important from the standpoint of the individual worker and the community remained long neglected by the medical profession as a whole. Interest on the part of medical men in this field has been rather sporadic. Most of the advances made till very recently have been made by sociologists, legislators, and economists, to whom the subject was ever of great importance. The medical profession as a whole has remained rather indifferent.

But very recently there has been a general awakening to the medical importance of the subject, and an intense interest is being manifested in various quarters in industrial diseases.

One of the factors which more than any other has helped to awaken this interest is the fact that the subject is receiving, as it were, academic sanction in many medical schools, notably at Harvard, where Dr. Edsall has been repeatedly emphasizing the importance of this field, and where a special department of Industrial Hygiene has been recently started and a journal devoted to industrial hygiene has been created.

Investigations into the effects of industrial hazards upon the health of the operatives exposed to them can, moreover, be made very fruitful, and should appeal to the research worker, for while we possess a considerable body of knowledge of the effects of industry on health, such knowledge is small compared with the problems which still await solution.

We have, it is true, some definite knowledge of the well-defined specific industrial diseases—the various industrial intoxications; the postural strains and localized fatigue effects manifested in the occupational neurosis.

We know, however, considerably less of the effects on the health of the operatives exposed to hazards which do not produce specific industrial diseases, but which nevertheless produce states of ill-health in which the industrial hazard clearly plays a prominent etiologic part. I refer to the hazards of non-poisonous dusts, of non-poisonous but irritating fumes, of extremes of temperatures, and of unsanitary conditions under which work is carried on, conditions which are not an integral part of the industry, but which are accidentally associated with it.

Our knowledge is still more meager when we consider the general effects on health from the factors more or less common to all modern industry—the stress; the speeding up caused by the machine-set pace; the monotony, mental and physical, caused by the great division of labor; and what seems to me is of vast importance, the general fatigue effects of industry. That these factors have no immediate effects that can be readily perceived and measured we know. They do not produce sudden, severe, incapacitating illness. They are not dramatic in their manifestations. But are they for that reason without effect? May not these factors to which the worker is exposed

throughout his working time gradually and insidiously undermine health and be responsible for the early development of the degenerative diseases of middle life—diseases which are coming more and more to the front as public health questions?

The limitation of our present knowledge of the effects of occupation on health is determined in part by the limitations of our physiologic and pathologic knowledge of certain problems; and in perhaps still a larger measure by our poor method of book-keeping. We have not kept accurate record of the relation of occupation to the train of symptoms which the worker complains of when he presents himself for treatment. For in our morbidity and mortality statistics we have not kept reliable records of the occupations. While death certificates provide for a statement of the occupation of the deceased, and hospital records contain statements of the occupations of the patients, the data are recorded in so unsatisfactory a manner as to give no indication of the actual work the deceased or the patient were engaged in. The general designation of the industry most often found on records, such, for instance, as rubber worker, shoe worker, textile worker, is not sufficient, for in the great variety of processes in any industry some have very definite health hazards, while others have no such hazards. To be of any value not only should the general industry in which the patient is employed be recorded but also the exact process the patient is engaged in.

This method of recording both industry and occupation has been adopted at the Massachusetts General Hospital in recent years. This detailed statement of the patient's occupation is in itself a great advance, and will in the course of time permit an analysis of the records according to the kind of work the patients were engaged in, and will permit deductions as to the relative frequency of certain diseases among any given class of workers. Were such a classification adopted by all hospitals and registrars throughout the country, it would in a very short time contribute an immense amount of knowledge as to the relation of industry to health.

A glimpse as to what interesting facts might be brought out

by an analysis of such statistics might be had by reading the summary made by Wynne and Guilfoy of the mortality in various occupations as shown by the returns to the New York Board of Health for one year. Small and insufficient as the data is, there are nevertheless many extremely interesting suggestions which point the way to further research.

Moreover, the recording accurately of the patient's occupation is not only important in hospitals, where, owing to the large numbers treated, statistics indicating the frequency of certain diseases among certain groups of operatives may be obtained, but is of great importance to the physician in handling his private practice, particularly when one practises in an industrial community.

A clear understanding of the patient's work will very often give a clue to the diagnosis of a case otherwise obscure, and frequently make an early diagnosis possible. The prompt and early diagnosis of occupational diseases is a matter of great importance both to the patient and to the community. To the former because prompt diagnosis will in most cases remove the worker from further exposure to the injurious agent, and thus minimize the possibility of very serious and even fatal injury. To the latter, that is, the public, the early diagnosis is important because occupational diseases are in a great measure preventable, and the prompt discovery of a case will, if proper measures be taken, prevent the occurrence of other cases. This responsibility of detecting the early cases and thereby preventing the occurrence of new cases rests entirely with the physician.

In 1914 in a paper on "The Early Diagnosis of Lead-poisoning" (Jour. Amer. Med. Assoc., June 6, 1914) I cited as illustrative examples a number of cases gathered from the Outpatient Records of the Massachusetts General Hospital which showed definite symptoms of lead-poisoning, and which, taking into consideration the lead hazard to which the patients were exposed in their work, should have made a diagnosis of lead-poisoning possible, and yet no such diagnosis was made because of the absence of a lead-line on the gums and of basophilic granules in the red blood-cells.

Since 1913 efforts at systematic study of industrial diseases have been made at the Massachusetts General Hospital. The work developed to such an extent that under the guidance of Dr. Edsall a special Industrial Clinic has been established, of which Dr. Wade Wright was in charge. When Dr. Wade Wright left for service the clinic was temporarily closed, but was recently reopened under the charge of the writer.

A trained assistant is placed every morning at the admitting desk of the Out-patient Department, and all cases employed in industries where there are any hazards are sent up to the Industrial Clinic for study. Special attention is thus given to the study and diagnosis of industrial diseases, which results in the discovery of cases which would have otherwise escaped attention in the general clinic.

In contrast to the cases referred to above, where diagnosis was not made owing to the failure to consider the hazards to which the patients were exposed, I wish to give you a few illustrative cases from the Industrial Clinic of how the diagnosis was frequently made because of the consideration of the hazard:

A man of forty-eight comes to the hospital complaining of attacks of epigastric pain, loss of appetite, and for the last ten days of diarrhea. There was no lead-line on the gums. Investigation disclosed the fact that as a shipbuilder he had been working for ten weeks in a lead-lined cold-storage room, and in his work he was exposed to lead dust and lead fumes. A diagnosis of lead-poisoning was made, which was confirmed later by finding lead in the urine and stools.

A plumber of forty-seven complains of attacks of abdominal pain radiating to the back. His appetite is poor; he has lost weight and he has pains in various joints. In spite of the absence of a lead-line, the symptoms and the lead hazard of his occupation pointed to a diagnosis of lead-poisoning. The diagnosis was later confirmed by finding lead in his stool.

A "spreader" in a rubber shop complains of attacks of abdominal pain which last a few minutes. He is very constipated.

A shipyard worker of thirty-five complains of pain in the lumbar region for three months.

A painter of thirty-one complains of loss of strength in his wrists and pains in his back and feet.

A painter of forty-eight complains of attacks of abdominal pain associated with constipation and dizziness.

An iron foundry worker of fifty-three has attacks of abdominal pain and constipation.

In all the above cases there were no lead-lines found, but inquiry into the occupations indicated the real lead hazard. The diagnosis of lead-poisoning was therefore made, and in every instance it was later confirmed by the finding of lead in the urine or stools, or both.

These cases illustrate the importance of considering the industrial hazard in the making of the diagnosis. Most of these cases would probably have escaped the diagnosis of lead-poisoning in a general clinic.

Unsatisfactory as is the situation in regard to lead-poisoning, it is still more unsatisfactory with regard to the less-defined industrial poisons. Absolute failure to correlate symptoms complained of by patients with the hazards of their occupation, even when such symptoms could not be explained by any of the physical findings, and would become perfectly clear if the industrial hazard were considered, was manifested to me several years ago when I looked up a number of patients exposed to naphtha fumes at their work.

Suppose a man presented himself to his physician complaining of attacks of dizziness, weakness, loss of energy and ambition, he tires easily, his appetite is poor, he has ringing in his ears, his speech is blurred at times, and he feels that he is losing his memory. Suppose the physician does not find anything on physical examination, but on inquiry into his patient's habits he learns that he is addicted to the naphtha habit—that to satisfy a perverse craving the patient inhales for several hours every day the fumes of naphtha. Would any physician fail under such circumstance to tell his patient that it was this perverse habit which brought about his state of ill health? Yet a man who actually presented himself with the above symptoms and who instead of inhaling naphtha fumes several hours

every day, inhaled it ten hours every day for six days in the week, not because of a perverse habit but out of necessity—he was cementer in a rubber coat factory, and while at work he was constantly bending over an open pot of naphtha cement—yet no diagnosis was made. The physician did not correlate the man's occupation and its health hazard with the symptoms of which the patient complained. All the symptoms cleared up on change of work.

A treer in a shoe factory suffers from dizziness, headaches, is sleepy and listless. Physical examination was entirely negative except for a mild secondary anemia. He inhales naphtha fumes, but the doctor who saw him did not realize the hazard, and made a diagnosis of constipation.

A driller in a watch factory complains of weakness, dyspnea, dizzy spells, loss of appetite, and insomnia. He has attacks of sneezing. A throat specialist, who saw him in consultation, gave as his opinion that the man suffered from "a peculiar vasomotor rhinitis," and the diagnosis made on the case was "constipation plus vasomotor rhinitis." Neither the throat specialist nor the medical man inquired as to what his work consisted of. If they had, they would have learned that to wash the plates he is working on, he squirts benzine from an oil can, and that many other men in the same room do the same work, and that the ventilation is inadequate to take care of the air so heavily charged with benzine fumes. Benzine-poisoning is a more intelligent diagnosis, one that explains the symptoms and the vasomotor disturbance, and one that would be likely to be of greater benefit to the patient.

A cementer in a rubber factory for six months complains of undue fatigue, headaches, nausea, and muscular twitchings. No diagnosis was made. At his work this man stands in front of an open bowl with naphtha cement.

A worker in a shoe-polish factory for six weeks, has not felt well for four weeks. Frequent attacks of vertigo, several attacks of vomiting; he suffers from frequent micturition. No diagnosis was made. This man was exposed to the fumes of turpentine at his work.

A man of twenty-three who worked as shoemaker in a rubber factory for two years, complains of headaches, attacks of dizziness, loss of appetite, bad taste in mouth, and constipation. These symptoms have been going on for a year and a half, but have become worse recently. The diagnosis that was made was that of constipation. This man uses naphtha cement constantly at his work. He works in a large room with 500 other workers in the same room, doing the same kind of work. The room is very warm. The windows cannot be opened for fear of drying the cement. It is quite evident that this constant exposure to naphtha fumes explains the symptoms perfectly well.

It is not necessary to multiply cases. The few I have shown sufficiently illustrate the evident fact that the failure to make a diagnosis in the above cases was due to the failure to take into account the occupation of the patients.

But the relation of industry to health is far broader in its scope than the specific diseases produced by industrial poisons. For, after all, the number of workers in industry who are exposed to industrial poisons is very small besides the vast army of workers who are exposed to dust and fumes and other conditions inimical to health.

Hoffman estimated that we have in this country at least 5,600,000 workers employed under conditions detrimental to health on account of atmospheric pollutions with dust and fumes, hazards which predispose or accelerate the development of tuberculosis and other diseases of the respiratory organs.

In a disease as wide-spread as tuberculosis it is, of course, difficult in any given case to state definitely that it is of industrial origin. The fact, however, that workers in certain industries give a higher death-rate from tuberculosis than other classes of workers living under similar conditions demonstrates very definitely that certain cases of tuberculosis are the results of industrial hazards. To take an illustration from Massachusetts' conditions. In the volume entitled "Tuberculosis in Massachusetts" Dr. Gordon, of Quincy, made a study of the occurrence of tuberculosis among the granite workers in that city. In a period covering ten years he found that the percentage of the

total number of deaths due to tuberculosis among granite workers was 46, while that of the rest of the community was only 16, which definitely demonstrates the very high death-rate from tuberculosis among that group of workers.

Dr. Gordon, however, made the extremely interesting observation that the mortality from tuberculosis among granite workers occurs later in life than is usual for the mortality from that disease among the rest of the community.

This condition is similar to the age distribution of deaths among miners, and quarrymen in the registration area of the United States, in that the highest mortality from pulmonary tuberculosis occurs among these workers between the ages of thirty-five to sixty-four, instead of between fifteen and thirty-four, the usual period of excessive mortality from tuberculosis.

If we consider, however, the mode in which the granite workers are affected, the reason for this high mortality from pulmonary tuberculosis later in life becomes clear. Stone-cutting is rather hard work and does not appeal to the physically weak. Those who start at the work are, therefore, apt to be in very good physical condition, and hence would have a natural immuntiy to tuberculosis. Long exposure to the irritating stone dust finally begins to produce changes in the lungs, the elastic lung tissue is replaced by scar fibrous tissue. This takes place gradually and insidiously, and may go on for a long time without giving rise to any symptoms. The fibrosis of the lung diminishes the resistance of the tissue and forms a favorable soil for the implantation of the tubercle bacillus. It is only then that infection takes place. It is after the fibrosis of the lung has broken down the natural resistance of the physically strong men who enter the industry that invasion with tubercle bacilli takes place. This seems to me to explain the late development of tuberculosis among that class of operatives and emphasizes the industrial origin of the disease.

But aside from statistical data pointing to the industrial origin of tuberculosis in certain industries, it is often quite easy in the individual case to estimate the effect the industrial hazard had in the development of the ill-health.

Here are a few illustrative cases from the Industrial Clinic of the Massachusetts General Hospital:

A man previously well and free from symptoms develops a dry, harassing cough immediately after starting work as a rag-sorter. There are no physical signs in his lungs to account for his cough. Rag-sorting, as you may imagine, is a very dusty work, and it is highly probably that his cough is the direct result of his dust inhalation.

A young man of twenty presents himself at the clinic with signs of advanced pulmonary tuberculosis. His father and two sisters died from tuberculosis. He started to work in a woolen mill as a carder at the age of sixteen and has been during the four years of his work constantly exposed to the dust of the carding machines. It does not seem as if there can be any doubt that the dust exposure, to say the least, accelerated the development of tuberculosis in a man so definitely predisposed to the disease. It seems as if it should have been somebody's job to prevent a young person with such a family history from entering such hazardous work.

A man of forty-three who worked at the carding machine in a woolen mill for twenty-seven years develops tuberculosis. He has no tubercular family history, his habits are good. Is it not highly probable that his dust exposure of many years' duration was the important factor in the development of the disease?

Dust exposure, however, is not the only hazard in industry which is responsible for tuberculosis or non-tuberculous disease of the respiratory organs. Among the hazards other than dust which frequently predispose to respiratory diseases are exposure to extremeness of temperature, more particularly exposures to sudden changes of temperature, as illustrated by the following cases:

A man of twenty-seven complains of frequent attacks of colds, with severe cough. He has lost some weight. His appetite is poor and he has occasional night-sweats. Physical examination is negative except for slightly increased signs in the right apex. This man is engaged in a wholesale fruit house and his job is to load teams with cases of fruit for transporta-

tion. The carrying of the heavy boxes causes him to perspire very freely, while perspiring he has to enter a cellar which contains huge ice-chests and is lined with ice-pipes. This process of getting chilled while perspiring is repeated many times during the working day and causes him to catch cold very frequently. He gave up work for some time on two occasions, during which time he felt much better, but the colds returned on his resumption of the work.

A man of twenty-five complains of pain in his left chest. He has a severe cough and raises a good deal of sputum, which is sometimes streaked with blood. He has frequent night-sweats and he has lost weight. His temperature is 100.4° F., pulse 110. There is diminished resonance in the tops of both lungs, over which areas the breathing is bronchial, with numerous râles. His sputum shows the presence of tubercle bacilli. For eight years this man has been working as a stoker on a steamboat. He is exposed to extreme heat, perspires freely while in the fire-room, and then goes on the deck where it is cold. His bunk is in a dark, damp, cold, and poorly ventilated room.

A woman of twenty-seven complains of frequent colds for the last six years, and a cough which is persistent without remission for the last two years. She raises a good deal of sputum, has night-sweats, and has lost some weight during the last year. The lungs show dulness at the right apex, with prolonged high-pitched expiration. *x*-Ray examination of the chest shows extensive peribronchial thickening.

She has been employed as a cook in a restaurant for ten years. For the last few years she has worked in a small kitchen without any windows in it, the only air coming into the room is from an adjoining dining-room. The room is very hot, she perspires freely at her work, and frequently has to go to the refrigerating room for supplies.

Cases could be easily multiplied where investigations into the patient's occupation revealed the probable cause of tuberculosis or non-tuberculous diseases of the respiratory organs.

Postural strains or localized strains are very often responsible for states of ill-health, as illustrated by the following cases:

A man of twenty-two complains of general weakness, poor appetite, pains in the lumbar region, and also in his right arm and leg. The pains have become so bad that he had to give up his work. Physical examination is entirely negative. This man came to this country from Portugal eleven months ago. He was a baker. He got a job here in a tannery washing skins. He works in a wet cellar. The work is very hard and disagreeable, and he feels that it has completely exhausted him. He was not physically fitted for such laborious work.

A woman of twenty-three complains of pain in her right shoulder and weakness of her right hand. The physical examination is entirely negative, except that the motions of the right shoulder are somewhat limited. This woman is working as a bone-puller in a fish loft; she pulls the side bones from cod-fish. There are 34 side bones in each fish, and she sometimes does as many as 130 fish an hour. It requires considerable pull to tear out the bones; she is engaged in this work for about five hours every day. The room where she works is very cold, and the fish is often so cold as to make her hands very numb. This case well illustrates the localized strain effects so often met with in industry.

In addition to these industrial hazards which are more or less inevitable in particular industries, though in many instances more adequate protection could be provided, there are conditions inimical to health found in industries which have no relation to the industry itself. I refer to the unsanitary conditions characteristic of certain industries. The unclean, poorly lighted, poorly ventilated workroom gives rise to no one disease, but reduces the resistance of the worker and keeps him in a state of impoverished health.

I have so far referred to the two main groups of diseased conditions arising from industry: (1) The specific industrial diseases, and (2) the diseases in which the industry acts as a predisposing cause rather than the immediate cause. There is still, however, another field about which we know little or nothing as yet. I refer to the general fatigue effects from the stress and strain of modern industry.

We unfortunately have no methods of measuring or estimating fatigue. We will have to learn a great deal more about the chemistry and the physiology of fatigue before we shall be able to demonstrate the baneful effect of chronic fatigue on the organism. But I firmly believe when the chapter on industrial fatigue is finally written that it will be found to play no small rôle in the causation of the so-called degenerative diseases of middle life.

At present our estimate of fatigue can be based only on observation of the quality and quantity of the output of the worker, and on the rate of the occurrence of accidents in industry. It is quite clear that the fatigued worker is not able to make as quick or as proper adjustments of his movements, or, as Ash demonstrated, the first symptoms of fatigue are an interference with the function of control over all kinds of motor expression, hence fatigue brings about an increase in the accident rate.

Some years ago I analyzed accidents that occurred in a large metal manufacturing plant for a period of ten years; there were several thousands of them. My analysis showed that the number of accidents increased every hour during the morning, reaching the maximum during the fourth hour and, curiously enough, declining appreciably during the last hour of the forenoon. I found the same to be true of the afternoon hours. That is to say, more accidents occurred between 10 and 11 than between 11 and 12 A. M., and more between 4 and 5 than between 5 and 6 P. M. This was to me a rather unexpected development, as one would naturally expect the greatest number of accidents to occur during the last hour of the morning or the last hour of the afternoon when, presumably, fatigue would be at its highest. This paradoxic discrepancy in the accident curve could not be explained by any change in the work or working force during the last hours of the morning and the afternoon periods.

In looking up later some statistics of accidents in European countries I found, curiously enough, the same conditions existed relative to the diminution of accidents during the last hour of the morning and the last hour of the afternoon.

This apparently paradoxic situation was found to be common to a great variety of industries carried on under different conditions. One is therefore forced to assume that this phenomenon must depend upon some fundamental factor in the economy of the organism. What this fundamental factor is still remains to be demonstrated.

Various explanations have been offered for the diminution of the accident rate during the last hours of the morning and afternoon working periods. None of the explanations thus far have been very satisfactory.

May it not be that this phenomenon is due to the fact that during the last hours of the working period the stage of physiologic fatigue has been passed, that all the energy available for the daily work has been exhausted, and that to meet the persistent demand the worker has to draw upon his reserve or potential energy which nature intended for use only in emergencies?

The existing fatigue, which is nature's call for a period of rest to replenish the exhausted energy, disappears when the stores of reserve energy are made available and the impairment of motor control, which is the first symptom of fatigue and which is responsible for the increase of accidents, disappears and the accident rate falls. This constant drain upon the reserve energy is comparable to the state of a person who lives above his income and has to draw on his capital. This constant use of reserve energy impoverishes the organism of the workers and keeps them in a state bordering on exhaustion, so that they are unable to withstand any emergencies, such as an attack by disease-producing forces. Whether this explanation is true or not it seems to me that there is a wide field of most useful and profitable research.

To summarize briefly: Industrial medicine in its wider meaning is a field primarily not for the industrial physician, but for the physician in the general practice of medicine. He must recognize that states of ill-health are in many instances due to the hazards of industry. Such recognition will often enable him to make an accurate diagnosis in an otherwise obscure

case, and through the aid of the health authorities often prevent the occurrence of other cases.

The field of industrial medicine is not only a profitable one for the clinician, but is a fruitful field for the research worker, for our knowledge in this important field is very small, and the problems that await solution are many and pressing.

CLINIC OF DR. LEWIS WEBB HILL

Children's Hospital

NEPHRITIS IN CHILDREN

Presentation of 3 Cases, and Discussion of the Differences Between Nephritis in the Child and in the Adult

February 17, 1919.

I wish to present today 3 cases of nephritis, and to discuss with you some of the differences between nephritis in the child and in the adult. These cases represent by no means *all* the types of nephritis that we see in childhood, but they are of especial interest because they differ considerably in many respects from cases of nephritis in older persons.

Case I.—Here is a boy, eight years old. He looks well, as you can see, save perhaps for slight anemia, and rather dark circles under his eyes. His *family history* is unimportant except for the interesting fact that his younger brother at home now is suffering from the same condition that he has himself. His brother was taken sick about a week after he was.

His *past history* is as follows: He has always been a strong, healthy boy, and has never had any of the contagious diseases except measles, which he had two years ago. His only illness has been tonsillitis, and during the last three years he has had two attacks which have lasted usually about five days. A year ago, after an attack, he suffered from swollen glands in the neck, which, however, disappeared in a few weeks.

His *present illness* began two weeks ago. At this time he had tonsillitis. The tonsils were much enlarged, showed white spots, and there was considerable prostration and fever. He stayed in bed three or four days with this, the throat cleared up, and he got out of bed feeling well. A day or two later his mother

noticed that his urine was bloody and that his face was a little puffy, so brought him to the hospital for treatment.

Physical examination shows a rather thin, pale boy, who does not seem very sick. The tonsils are not at present large, but are rather lobulated, inflamed, and unhealthy looking, with large crypts. His teeth are good. On each side of the neck there are two or three small, hard, non-tender lymph-nodes, the size of marbles. The heart, lungs, and abdomen are negative. There is no edema anywhere. Here is a specimen of his urine, and I think you will all agree that it is unusually bloody, even for a case of acute nephritis; it looks almost like clear blood, and there is a heavy dark red sediment in the bottom of the tube. It contains a large trace of albumin, and microscopically shows large numbers of red blood-cells, many small round cells, a few pus-cells, and a very rare granular cast. The phthalein test is 55 per cent. The blood urea nitrogen is 14 mgm. per 100 c.c. blood (normal).

The two-hour renal test (see Case II) shows a decided fixation of specific gravity, at a low level, as follows:

Time.	Specific gravity.
6–10	1015
10–12	1016
12–2	1015
2–4	
4–6	1015
6–6	1014

At no time has there been any edema, and on a daily fluid intake of 48 ounces he passed usually from 28 to 38 ounces of urine.

His systolic blood-pressure is 98, the diastolic 60.

Discussion.—This boy, I think you will all agree, does not present the picture of our ordinary text-book conception of acute nephritis. His urine secretion is good, he has no edema, the blood-pressure is normal, he does not seem sick, and his urine contains an extraordinarily large amount of blood, but very few casts.

It is a streptococcus condition, probably a glomerulonephritis, and is due possibly to damage of the glomerular vessels by

the streptococcus toxin, or perhaps to their actual invasion and occlusion by the streptococcus itself. It is seen in adults, but is not, I should say, the ordinary type of nephritis from which they suffer. It is, however, the most common type of nephritis that we see in children and is almost always secondary to tonsillitis. It should be called "acute hemorrhagic nephritis," and its distinguishing features are lack of marked edema and a very bloody urine containing *very few casts*. Indeed, I have seen physicians who were not familiar with children doubting the occurrence of nephritis at all, on account of the scarcity of casts, and searching for some other condition which would cause hematuria, such as renal stone. The importance of tonsillitis as a cause of nephritis is not usually recognized, but it is, in children, at any rate, a much more common cause than all the other infections combined, not excluding scarlet fever. The nephritis starts usually not during the tonsillitis, but anywhere from a few days to two weeks after the acute throat symptoms have subsided. It lasts in most cases from four to twelve weeks, but occasionally small amounts of albumin and of blood may persist in the urine for many months. A few patients ultimately develop chronic nephritis, from which they finally die, but it is rare for a fatal outcome to occur during the acute stage. Functional tests are moderately diminished, but rarely to the extent that they would be in the ordinary text-book type of acute nephritis in adults. The phthalein test in this case would be normal for an adult, but low for a child, the lowest normal limit for children being about 60 per cent. The two-hour renal test shows an abnormal response; normally there should be a wide difference in specific gravity between the two-hour specimens. The blood urea is normal. In this particular case the functional tests are interesting, but not particularly valuable, as we know from the boy's general condition that his kidney function cannot be much diminished. In fact, as far as treatment goes, we could handle this patient exactly as well if we had not done the functional tests. In chronic nephritis they may be of considerable value, as we shall see in the next case.

How shall we treat this boy? In the first place, he should

be kept quiet and warm. He should not get out of bed for anything, and should be wrapped in an extra blanket. Exertion and cold are two of the worst things a child with acute nephritis can be subjected to. He should have one good bowel movement a day, but there is no necessity for purging him, as his urine secretion is good, and he has no edema. In these hemorrhagic cases without edema it is well to give as much fluid (within reason) as the patient can handle, as it is probably of value to flush the kidneys and aid in diluting and in eliminating toxins. This boy has been taking 48 ounces of fluid daily, as you can see from his chart, and has handled it well, as his urine secretion is about what it should be, and he has not gained in weight. The diet is important, and here again we need to restrict him very little. There is no edema; therefore there is no good reason for giving him a salt-free diet, although we should be careful, on the other hand, not to let him have an excessive amount of salt. The greatest prinicple in treating any case of acute nephritis is to spare the kidneys as much as possible. Although it is possible that this boy's kidneys might be able to handle a large amount of protein waste, it is only reasonable to cut his protein allowance to the minimum amount which will cover the nitrogenous needs of his body. We have no very clear idea what the nitrogenous needs of young children are, but we know that they are greater than those of adults, and if we give this boy about 2 gm. of protein for each kilogram of body weight we shall probably keep him in nitrogenous equilibrium. You will see from his chart that in the hospital we have the nurses calculate carefully the total calories and the protein of his diet, but in private practice this is not necessary. If, during the acute stage, while the urine contains considerable blood, meat, eggs, and meat soups are omitted, and the diet is made up of milk, cream, butter, cereals, vegetables, and fruits, we shall come very close to what is desired. The only drug that is of any value is iron, to compensate as much as is possible for the large amount of blood that is lost daily in the urine, and this boy has been having 5 grains of the saccharated oxid of iron three times a day, which is perhaps the best form of iron to use with children.

We shall begin to think of letting him up when his urine contains only a rare red blood-cell microscopically, and no albumin, or the slightest possible trace. If considerably more blood appears in the urine after he has been up, and persists, he will have to go back to bed again. Many of these cases may show a very small amount of albumin for a considerable time, and it may not mean much, but if the blood persists, even microscopically, the patient should be treated very carefully, and should be kept in bed most of the time.

When is the best time to take out the tonsils? Some observers advocate doing this immediately, and some say to wait until the nephritis is entirely recovered from. Personally, I believe a middle course is best, and should advise tonsillectomy for this boy as soon as the acute stage has passed and his urine contains only a moderate amount of blood.

CASE II.—The next case presents a somewhat different problem. This girl of ten was brought to the out-patient department of the hospital with the following history:

Family history unimportant.

Past History.—Measles at one year, diphtheria at seven years, no scarlet fever, pneumonia, rheumatism, chorea, or tonsillitis. She has never been a very strong child, but has been apparently well up to the onset of her present symptoms.

Present Illness.—For the last year she has been pale and weak, and gets tired very easily. Her appetite is poor, and she has gained only a pound in a year. No cough. Has slight dyspnea and palpitation on exertion. No precordial pain. No nocturia, polyuria, dysuria, or hematuria. No excessive thirst, no enuresis.

Physical Examination.—Shows a rather thin, washed-out looking girl, rather tall for her age, and standing with a marked lordosis. Her head is negative. The eyes are normal. The nose is negative. The tonsils are not large and are apparently normal. The teeth are poor, and a definite pus-pocket can be seen on the gum at the root of one of the lower premolars. The tongue is heavily coated, and the breath, though not very foul, is rather unpleasant. There is no general glandular enlarge-

ment. The heart measures 2.5 x 8 cm., the sounds are of good quality, and at the apex there is heard a short, soft, and rather insignificant systolic murmur, which has only a very narrow area of transmission ("functional"). The pulmonic second sound is greater than the aortic second. The lungs are negative. The abdomen and extremities are negative. There is no edema.

Diagnosis.—We see many such children in the out-patient department, and the vast majority of them with the symptoms that this girl complains of are suffering from no definite disease, but simply from the wrong sort of food, hygiene, and home conditions. We have not completed our examination in such a case as this, however, until we have looked at the urine. The urine is clear, with a specific gravity of 1022. Contains a slight trace of albumin, no sugar, and has an occasional hyaline and granular cast in the sediment, with a few blood-cells. Here we have, then, probably either a mild chronic or subacute nephritis, or possibly postural albuminuria, and we have found a definite cause for her symptoms. She was sent into the wards for study. If she has a postural albuminuria the urine should be free from albumin while she is kept in bed, and should contain albumin when she is up and around, particularly if she is up and the lower part of her body is immobilized. The general appearance of the patient and her very evident lordosis would suggest this. She was put to bed, and several urine examinations were done while she was in bed at different times, and while she was up and around, with the following results:

Specific gravity.	Albumin.	Sediment.
Up—1009 (quiet).	S. T.	Rare hyaline cast, and a few red blood-cells.
In bed 1—10015.	S. P. T.	No red blood-cells or casts.
In bed 2—1018.	S. T.	Rare granular cast.
Up and moving—1022.	L. T.	Rarely a granular cast.
In bed—1018.	V. S. T.	Few red blood-cells and casts.

It would seem that she has, therefore, not a postural albuminuria, but a chronic nephritis, as staying in bed did not render the urine albumin free.

Discussion.—My reason for showing this child is to call especial attention to the fact that many cases of chronic neph-

ritis in children may be of a very mild character, and present a totally different picture from chronic nephritis in the adult. We see in children many times the "chronic parenchymatous" nephritis of the adult, with the severe anemia, extensive edema, etc., and usually can suspect the diagnosis from the appearance of the patient, but there is nothing in this type of case to suggest nephritis until we examine the urine. Occasionally, if these children happen to pick up an acute infection of any sort, they show an exacerbation of the nephritic condition, but they rarely have much edema or seem very sick. The blood-pressure is not elevated (indeed, it is likely to be lower than normal) nor is the heart hypertrophied. The urine ordinarily shows only a small amount of albumin, with a rather insignificant sediment, in which a few casts of the granular and hyaline varieties and an occasional blood-cell may be seen. There is always the necessity, in these mild cases, of differentiating the condition from postural albuminuria, and this can be done, as it was in this case, by examining the urine for albumin a number of times while the patient is in bed, and again while he is up and around. In postural albuminuria the second and succeeding specimens passed after the patient has been put to bed should always be albumin free, and we cannot make a diagnosis of postural albuminuria unless this condition holds. So far as I know, there is no condition in the adult which corresponds to this type of nephritis. You will note particularly that there is no hypertrophy of the heart, and that the blood-pressure is not elevated; occurrences which help us a good deal in the diagnosis of chronic nephritis in the adult. In the child these signs may occur, and are of value in diagnosis if they do, but are more often absent than present in this mild type of case. In this particular case the etiology is obscure; there is no history of a preceding acute nephritis, although it is possible that her kidneys may have suffered injury during her diphtheria three years ago, or that the abscess that she has now at the root of one of her teeth may have something to do with it. The tonsils appear harmless, but may contain pus-pockets.

What we wish to know particularly about this girl is the

extent of damage that has been done to her kidneys. From her general appearance we should infer that they have been little damaged, but the functional tests may help us in deciding this, and it is in just this type of case that they are sometimes of value. Here again we must contrast the adult and the child. In the adult high or normal functional tests in a case of suspected chronic nephritis would almost certainly indicate to us that the kidneys were little damaged. In the child this is not necessarily true, and I have seen several severe chronic cases with normal phthalein tests and normal figures for blood urea. The "two-hour renal" test, as elaborated by Mosenthal, which I have used with children in a somewhat modified form, is more reliable, and I have seen few cases of well-established chronic nephritis which did not show deviations from the normal. Low phthalein excretion, high blood urea, and abnormal two-hour tests give very reliable evidence, on the other hand, that the kidneys are severely damaged and that the prognosis is poor.

This girl had a phthalein of 65 per cent., which is normal, but does not help us much one way or the other. The "two-hour" test is valuable and extremely simple. The child is put on a full diet containing plenty of meat, with 10 ounces of fluid at each meal. She is also given 2 grains of caffein sodium benzoate and about a gram of salt with each meal. For the sake of uniformity, in the wards we use the following diet, but it is not at all necessary that the child take all of it, or that it be measured carefully or weighed. It is essential that no fluid or food be taken between meals, and that the same amount of fluid is taken at each meal.

Breakfast:	*Dinner:*
Cereal, 2 tablespoonfuls.	Chopped meat, 2 tablespoonfuls.
Bread, 1 slice.	1 egg.
Butter, ½ square.	1 potato.
Apple sauce, 2 tablespoonfuls.	Butter, 1½ cubes.
Milk, 6 ounces.	Milk, 6 ounces.
Water, 4 ounces.	Water, 4 ounces.
Extra salt, 1 gram.	Extra salt, 1 gram.
Caffein sod. benzoate, 2 grains.	Caffein sod. benzoate, 3 grains.
Supper:	
Same as breakfast.	

The urine is collected at two-hour intervals, and the specific gravity of each specimen is taken. Normally there should be a variation in gravity of the different specimens of 8 points or over between the highest and the lowest. This indicates that the kidneys have the power of varying the concentration of the urine according to the demands made upon them. In damaged kidneys this power is lost, and there is very little difference in gravity between the two-hour specimens. Sometimes all the specimens may show almost exactly the same specific gravity. this girl had a normal two-hour test, as follows:

Time.	Specific gravity.
6–8	1019
8–10	1006
10–12	1020
12–2	1021
2–4	1028
4–6	none
6–6	1022

As criteria of the efficiency of this particular girl's kidneys we can include:

1. Her general condition.
2. The character of her urine.
3. The two-hour renal test.

Her general condition is certainly not compatible with a severe kidney damage. Her urine shows a comparatively small amount of albumin and few casts, and her two-hour test is normal. We may, therefore, say that she has not enough damage to her kidneys at present to materially interfere with their functional efficiency.

Just what will happen to this girl? Will she rapidly develop a diffuse severe chronic nephritis and finally die from it? Will she slowly develop a contracted kidney, and have ten or fifteen years from now what is called "chronic interstitial nephritis," or will she finally get over her nephritis entirely?

The first possibility is, I think, unlikely. It is quite likely that a good many of the cases of chronic interstitial nephritis that we see in after-life may have had their foundation on some

such basis as this, and it is possible that this child may slowly develop a contracted kidney. On the other hand, it is not at all unlikely that her albuminuria will gradually disappear, and in a few years she may have a perfectly normal urine.

How should she be treated? The two most important things for her to remember are to avoid infection and overexertion. Her teeth should be put in order by a competent dentist and her tonsils should probably be removed. She should avoid chilling and exposure. She should not go in bathing, she should engage in no violent sports. These are the main things to bear in mind; the diet in such a case as this is entirely secondary. It would be quite wrong to put this girl on a closely restricted diet —she should have meat once a day, she need not particularly avoid salt, and for the rest of it may have about what would be a rational, normal diet for any girl of her age. I should give her 5 grains of the saccharated oxid of iron thrice daily, and also the following prescription which we use a great deal here at the hospital:

℞. Nux vomica..... ℥ij
Glycerinated elixir of gentian..... ℥vj
Sig.—One teaspoonful before each meal.

Case III.—This boy of seven represents a very rare condition in childhood—*chronic interstitial nephritis*, which merits a brief discussion on account of its rarity.

The *family history* is not remarkable. His father and mother are both apparently in good health. He is an only child and there have been no miscarriages.

Past History.—He has never been a robust child, and has always been somewhat thin and undersized, but has been considered healthy by his parents except for the "attacks" for which he enters the hospital. He has had no acute infectious diseases.

Present Illness.—Since he was a year old he has been subject to "bilious attacks," which have been becoming more frequent in the last two years. Previous to two years ago one would occur perhaps every month or two. In August, 1916, he began to have them once a week; for the last few month he has had an average of two attacks a week. The attack usually starts

at night. He wakes up at 3 or 4 A. M. with headache, crying with the pain. After an hour or two he begins to vomit. The attacks usually last from twelve to twenty-four hours, after which he is fairly comfortable, with the exception of an occasional moderate headache, until the next one. The attacks seem to bear more relation to overfatigue than to food. He is very thirsty always—drinks a large amount of water and passes a great deal. Dr. S., the family physician, has examined the urine three or four times during the past year, and has found it normal at every examination, until a few days ago it was found to contain $\frac{1}{20}$ per cent. albumin and a few pus-cells in the sediment. It contained no casts or blood. For the last two months his headaches have been nearly continuous and of extreme severity, so severe that at another hospital his head was *x*-rayed with the possibility of a pituitary tumor in view. Two months ago on account of poor vision he was taken to an eminent oculist, who examined his eyes and said that there were one or two small spots on the right retina near the disk. He prescribed glasses, but made no diagnosis of any cerebral or severe ocular condition. The glasses did not help him at all. The "bilious attacks" have been so frequent for the last month that he has been in bed with them most of the time. A week ago, according to his family physician, there was a good deal of blood in his urine. Four days ago he was taken to the same oculist he went to before, who reported a diffuse retinitis of both eyes, which he said looked albuminuric. The next day he entered the hospital for study.

Physical examination shows a pale, very much underdeveloped boy, weighing only 37 pounds. The pupils are equal, regular, and react to light. Both retinæ show a diffuse retinitis. The tonsils are small and appear normal. The heart is slightly enlarged, but there are no murmurs. The aortic second sound is decidedly louder than the pulmonic second and is definitely accentuated. The lungs are negative, as is the abdomen, and the liver and spleen are not felt. The genitalia are small and much underdeveloped. The knee-jerks are equal and active. There is no edema. The urine has been examined several times, and has always been of low gravity (1010 to 1014), has con-

tained very slight traces of albumin, and at most examinations rare granular casts and a few blood-cells. The phthalein test is 55 per cent. (definitely low for a child). The systolic blood-pressure is 210, the diastolic 120.

Discussion.—This condition is apparently the same thing as "chronic interstitial nephritis" in the adult. It is very rare in children, and not more than 20 or 30 cases have been reported in the literature. The etiology is very obscure, and in some instances seems to be of a familial tendency, as there are cases on record where two or more children in the same family had the condition. Syphilis probably is not an etiologic factor. The most striking and interesting characteristic of the condition is the occurrence of infantilism, and nearly all of these children are very much underdeveloped both mentally and physically. The symptoms are those of chronic interstitial nephritis in the adult. The blood-pressure is usually very high, the heart is hypertrophied, headaches, visual and gastric disturbances are common, and there is polyuria and polydipsia. The urine is of constant low gravity, contains a small amount of albumin, and a rare cast or blood-cell in the sediment. The urinary changes, aside from the low gravity, are often so slight as to pass unnoticed, and it is possible (as in this case) to make several urine examinations, and to find nothing abnormal save the low gravity. The disease is so rare that if one does not have it in mind it may be overlooked. The blood-pressure is the best single guide, and it is always advisable to take blood-pressure readings on any underdeveloped child with headache or visual symptoms. At autopsy the kidneys are very much shrunken in size, and histologically show the typical changes of "chronic interstitial nephritis. This is the only form of nephritis in early childhood in which the blood-pressure is constantly high, and in which the cardiac hypertrophy is enough to be of any diagnostic value. In other types of nephritis in children, both acute and chronic, the blood-pressure may be high or normal, and is, therefore, not of the same diagnostic value that it is in the adult.

The prognosis of this condition in children is always bad, and the chances are that this boy will live only a few months at best.

CLINIC OF DR. FRANKLIN W. WHITE

BOSTON CITY HOSPITAL

IMPROVEMENT IN THE MEDICAL TREATMENT OF CHRONIC ULCER OF THE STOMACH AND DUODENUM

General Principles of Treatment.—We will first outline the principles of treatment and then give the details of our routine. We are always somewhat at a loss in treating a disease of whose exact cause we are not sure. The latest trend of opinion favors an infectious origin. Rosenow and others have produced ulcer by bacterial infection, and we now try to root out all sources of infection in ulcer cases. We clean up pus-pockets about the teeth and tonsils and sinuses, as well as remove an infected appendix or gall-bladder. This is good for ulcer patients and for anyone else, and we have been very scrupulous about it for the past few years. It is too soon to judge end-results. Our impression is that recurrences are less common where this is done.

Whatever the origin of ulcer, whether infectious or not, we want to know *what keeps it from healing and makes it chronic.* This has been well established both by experimental work and observation of patients, and serves as a working basis for treatment.

The most important factor which retards the healing of ulcer is delay in emptying the stomach. A second factor is the presence of an abundance of free acid. A third factor is mechanical, the irritation of the ulcer by peristalsis, spasm, and food particles. Therefore in order to heal a chronic ulcer we must avoid everything which increases gastric acidity, peristalsis or spasm, or the total work of the stomach.

We must use bland foods which cause least acidity, least

secretion, least peristalsis, and leave the stomach quickly, and use other measures which reduce secretion, peristalsis and spasm, and promote emptying of the stomach (sedatives, atropin, lavage, etc.).

We must especially relieve pyloric spasm, which is a far more common cause of retention of food than tissue narrowing.

There is no question that psychic influences, nervous shock, mental strain, and overexertion play an important part in developing and continuing ulcer. This is no doubt brought about by increased spasm and increased secretion of gastric juice. We must rest and build up our patient and teach him to avoid emotional excess and try to change his faulty mental habits.

Above all, we must *individualize the treatment;* all ulcer cases can no more take the same treatment than all diabetics can eat the same diet. We must treat the ulcer according to its position and size and the changes in function which go with it. The treatment is an experiment to be watched and followed, like increasing the diet in a diabetic.

We can be more patient with the *duodenal* than with the gastric ulcer, and continue the treatment longer in the face of difficulties, for we have not the fear of cancer hanging over us.

We can afford to try medical treatment in the *small gastric ulcer*, while with the large one we prefer to call a surgeon. Some men consider the demonstration of *any* ulcer in the stomach as an indication for a surgeon. We do not agree. If the surgeon tries to excise every ulcer of the stomach regardless of size or location, more patients will die of operation than of cancer.

The *ulcer with retention of food* needs special attention. It is on the borderline between medicine and surgery. We must relax spasm of the pylorus by the free use of atropin, or, if need be, remove the contents of the stomach at bedtime with the tube, and do everything possible, including rest in bed, hot compresses, and alkalies, to reduce irritation, infiltration, and edema about the ulcer. Here we must get prompt and definite good results from medical treatment, otherwise the case is surgical.

Our only excuse for using medical treatment in these cases

is the fact stated by Dr. W. H. Mayo years ago, that *delay in emptying the stomach in chronic ulcer is due to actual tissue narrowing in less than 10 per cent. of the cases.* It is very important to decide whether delay in emptying the stomach is due merely to spasm of the pylorus or to actual tissue narrowing. I want to emphasize the use of atropin in deciding this question. Many a case of obstruction, which we believe at first to be organic, relaxes almost entirely under the use of atropin and other treatment. This is well illustrated by our first patient.

CASE I.—Mr. R. C. P. C., age sixty-nine; a very hard-working engineer, has had a mild diabetes for ten years, easily controlled by diet. He had attacks of indigestion in 1900, 1906, 1912, 1918, lasting a few weeks to several months, with intervals of good health between. During his recent attack, which has lasted a month and which is like the previous ones, he has had epigastric distress or pain chiefly between meals, with heartburn and acid regurgitation. There has been no nausea and no vomiting. He has used the usual diabetic diet of eggs, meat, fish, and some green vegetables and fruits, with a small amount of bread and cereals. He has had a blood-pressure of 190 to 200 for about five years, with rare headaches and dizziness. His average weight has been 148 pounds up to three months ago, and he now weighs 133 pounds. He is a well-preserved old man; with good teeth, his tongue is fissured; the heart is somewhat enlarged. There is nothing to be found in the ordinary examination of his abdomen. His urine shows a slight trace of albumin and 1 per cent. of sugar. His stomach, after a test-breakfast, showed low normal secretion, Free HCl 20; total acid 39; no mucus; no blood with benzidin. The amount removed from his stomach after a test-breakfast was 329 c.c., showing that very little of the meal had passed the pylorus.

The Roentgen examination showed a stomach of smooth outline, with active peristalsis; a deformed duodenal cap which I was never able to fill out even under a long fluoroscopic examination and series of plates. Very little of the barium meal had passed out of the stomach at the end of six hours, and at

the end of twelve hours fully half of it still remained in the stomach.

The diagnosis of duodenal or pyloric ulcer was made, and in spite of the very marked obstruction medical treatment was begun—such as rest in bed, hourly feedings, alkalies, and atropin—with the hope that a great deal of the obstruction was due to spasm and inflammatory edema and would promptly subside. I thought the possibility of cancer was remote, but the stools were tested every few days for blood. They were found negative after the first four or five days.

Under this medical treatment he made an uninterrupted recovery, gained about 15 pounds in weight, and has had absolutely no gastric symptoms for a year.

This case shows how marked an obstruction may be present as a result of secondary spasm of the pylorus associated with an ulcer nearby, and how completely this type of obstruction may sometimes be relieved by appropriate medical treatment.

The patients with a *good-sized gastric ulcer*, with a crater as wide as a 5-cent piece, well up on the lesser curvature, who refuse operation, are a trying class. Medical treatment sometimes gives excellent results, but we always feel as though we were playing with fire, and the patient may remain only partially well. (See Case V.)

In the *ulcer which bleeds* everything must be sacrificed to stop the bleeding, and the case overhauled and classified later.

Last, but not least, people differ greatly in their general make-up and ability to tolerate an ulcer. The patient must be treated as well as the ulcer.

Hospital patients often require surgical treatment of ulcer when private patients would not, because the former are unable to favor themselves by rest, good hygiene, and a carefully selected diet for a long period.

Follow-up System.—I want especially to emphasize the *need of a good follow-up system* in chronic ulcer. This is just as necessary as in diabetes. These ulcers are essentially chronic. This should be carefully explained to the patient. The greatest failure I see in medical treatment is the lack of following the

cases carefully for months and protecting the stomach from irritation for a long time.

Every ulcer is different from the last, and every medical treatment is in the nature of an experiment, and needs careful watching and frequent modification. There is no such thing as "the ulcer treatment" any more than "the diabetic diet." We do not want to lose track of a case of diabetes and only have him report when there is sugar in the urine, neither do we wish to lose track of a chronic ulcer and only have him report when his symptoms are severe. To watch the patient with chronic ulcer and protect him from recurrence is just as much our business as to keep the diabetic sugar free.

We do not depend simply on the patient's symptoms and general condition, we use the Roentgen ray freely to *watch the anatomic changes in the ulcer and their effect on gastric function.* In our follow-up system we emphasize the following points: Blood tests of the feces are made every few days at first until the stools are persistently negative. After convalescence, in addition to regular reports at intervals on general condition, symptoms, weight, etc., we make a Roentgen-ray examination of the patient at the end of three or four weeks, and at intervals of three or four months for a year or more after this, depending on the case, in order to study the anatomy of the ulcer, changes in size, peristalsis, persistent spasm, the emptying of the stomach, etc.

Of the occasional functional tests, the motor test is the most important. We use the fluoroscope personally because we usually combine the motor test with the observation of the ulcer itself. The general practitioner will naturally use the stomach-tube for the motor test. It is, of course, much simpler and more readily available. This is not the place to discuss the relative value of barium meals and ordinary meals in testing the motor power of the stomach. They run closely parallel, as a rule.

The response of the patient to treatment as shown by symptoms, motor tests, blood tests, and the anatomy of the ulcer soon gives us a clue to the expectation of cure. This observation of the patient has great value in protecting him from

cancer. It is safe to say that in nine-tenths of the ulcers which "go bad" cancer could be avoided by an efficient follow-up system and constant weeding out of cases unsuitable for medical treatment. Not a single unpleasant surprise of this kind has occurred in our ulcer cases since this follow-up system has been carried out.

A follow-up system is equally valuable in cases after operation. In addition to judging the case by general condition and symptoms, we can decide by Roentgen examination about the anatomy of the ulcer, whether or not the new opening is working well, if it is in the right place, or too large or too small, whether or not food goes freely and promptly through it, whether the stomach empties too fast or too slowly, whether the cutting of circular fibers has hurt the muscular action of the stomach and caused food to pile up in the lower end of the stomach below the opening, and whether adhesions are present. More than one examination is usually needed when stasis, spasm, or pocketing is found. These changes are often variable and may entirely disappear after the use of atropin. Neglect of this rule has led to wrong opinions about the stomach and its functions and sometimes to needless secondary operation.

We must have all this data to decide what later treatment is best for the individual case. We have frequently been able to quiet the fears of the patient, lest something had gone wrong with the mechanism of the stomach after operation by demonstrating normal, smooth emptying, and then have stopped the symptoms of irritation by simple medical treatment.

This *medical treatment of ulcer cases after operation* is very important. The surgeon frequently tells his patient after operation that he is now perfectly well and can do anything he likes. I have met this statement again and again, and it is rarely true. The ulcer case with gastro-enterostomy or excision is "damaged goods," and frequently needs some medical advice in order to keep well. I have a long and steadily lengthening list of ulcer patients who need help *after* operation, usually after gastro-enterostomy; not in the first week or few months after operation, but six months or more later. The old symptoms return—

acidity, distress, pain, vomiting—and the patient fears another ulcer, perhaps another operation. Examination almost invariably shows that the patient has become careless in various ways in regard to diet, mental strain, tobacco, or alcohol. Frequently the examination shows a tendency to hyperacidity and spasm and active peristalsis. The stomach is usually empty in the normal time. We have an irritated stomach, not another ulcer. A short course of ambulatory medical treatment has almost always checked these symptoms and brought about a return to health which lasts as long as the patient uses care. I firmly believe that some regular medical advice and follow-up system is desirable in all surgical ulcer cases.

Let me emphasize once more in closing this paragraph on the follow-up system, that chronic ulcer must be considered a serious chronic disease which produces years of individualism and frequently threatens life. It becomes us to take it seriously and *watch the patient carefully for long periods* and neglect no important details which will help him to get well.

It sometimes appears as if there were real *differences of opinion between physicians and surgeons about the treatment of ulcer*. These differences are not real. They are due almost entirely to the difference in the material seen. The earlier and simpler cases come to the physician, the later, more severe and complex cases, are selected for the surgeon to see. Sometimes the surgeon is a little intolerant of any medical treatment of chronic ulcer because he only sees the class of cases in which medical treatment has failed.

Medical treatment, properly used with the new and more exact methods we now have for diagnosis and observation, will cure more chronic ulcers than surgery. Not necessarily because it is a better treatment, but because it is always used first. We must choose our case for medical treatment with care and good judgment, and remember that surgical treatment begins where proper medical treatment leaves off. There is always a good-sized group of cases which we cannot permanently cure by medical means, and we owe a great debt to the surgeon for the development of a successful treatment for the difficult cases of chronic ulcer.

The surgeon sometimes twits the physician with the fact that his "cures" are not all cures, some of them are simply remissions.

What are the signs of cure of an ulcer? A long period of freedom from symptoms, say six months or more, the longer the better, combined with normal gastric functions, absence of blood in the stools, and a marked or complete change in the anatomy of the ulcer (filled up crater, normal peristalsis, no spasm or hour-glass contraction). When an ulcer reappears after such an event, I think we are justified in calling it a *new* ulcer, not the recurrence of an old one. Ulcers in hospital patients recur much more frequently than in the well to do on account of coarse diet, alcohol, hard work, and unfavorable conditions, and therefore need surgery more often.

The **anatomic results of medical treatment of ulcer,** as judged by the Roentgen examination of the patient, are very interesting. They are most easily studied in the ulcers along the lesser curvature which have a definite crater, perhaps some spastic hour-glass deformity, and also in ulcers of the duodenum where there is a characteristic deformity. We have seen the crater of gastric ulcer along the lesser curvature entirely disappear in several cases after medical treatment, but thus far we have not seen a single markedly deformed duodenal cap which has entirely filled out to its former smooth, plump contour after treatment. Evidently a certain amount of scar tissue or adhesions have persisted which still deform the delicate walls of the duodenum. This is true even in cases which have remained entirely without symptoms for a year or more, and which we considered cured. The deformity of the duodenum has greatly lessened, but *not entirely* disappeared. In ulcers at the pylorus without definite crater and with a good deal of induration and scar tissue the anatomic changes after treatment are not striking.

Even in healed ulcers along the lesser curvature the scar tissue usually gives a small, smooth, rigid area over which peristaltic waves do not run.

We must give just a word of warning about using the Roentgen ray to study the anatomy of the healing ulcer. We must be very careful and thorough with the Roentgen examination

and use the fluoroscope as well as take plates for record and for detail. We must not be misled by variations in appearance caused merely by different degrees of filling the stomach and duodenum or different angles at which pictures are taken. It is even possible that food may occasionally stick in the bottom of an ulcer crater and make it appear shallow. Ulcers are usually less well seen after a gastro-enterostomy, as the barium meal may run rapidly out of the new opening, leaving the stomach only partly filled.

FIG. 242.—Normal duodenal cap for comparison (life size).

FIG. 243.—Normal duodenal cap for comparison (life size).

These difficulties can be overcome with care. We believe that the Roentgen examination, which has proved so very helpful in diagnosing ulcer, can be equally useful in watching the results of treatment.

The ulcer deformity *in postoperative cases* as viewed by the Roentgen ray behaves in much the way it does after medical treatment. That is, deformity of the duodenum and pyloric region persist to a greater or less degree in ulcer of the duodenum and pylorus, and usually is distinctly less than when first examined. The deformity in ulcers of the lesser curvature

frequently disappears almost entirely in a short time; in others areas of adhesions and scar tissue persist.

Out of a group of about 30 *medical cases* which have thus far been followed for a year or more after medical treatment I have chosen a few to illustrate these points.

CASE II.—Dr. H. A. C.; age forty; in hard general practice; had an infected tooth root and an infected antrum. He has had typical hunger-pains and soda habit, with rare night pain,

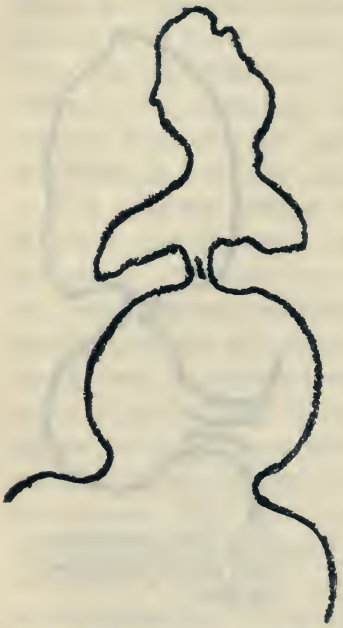

FIG. 244.—Case II. Duodenal ulcer (life size).

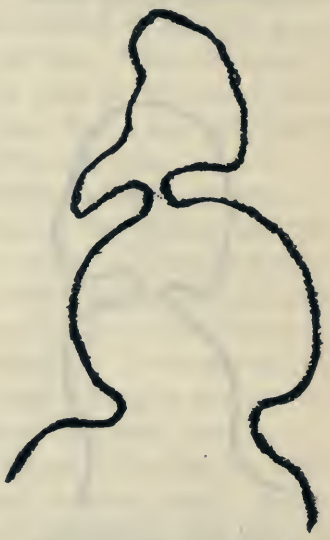

FIG. 245.—Duodenal ulcer, one and a half years later, medical treatment free from symptoms for over a year, some deformity persists (life size).

intermittently, for three or four years. His stomach contents showed very marked hyperacidity, and Roentgen examination showed a deformed duodenal cap as seen in Fig. 244. Compare with Figs. 242 and 243 of normal duodenal caps. The stomach emptied in the normal time.

After taking ambulatory medical treatment of the ulcer he has remained entirely well for a year and a half.

We still have the deformity which is shown in Fig. 245. The

duodenal cap is still very hard to fill, and there is a kink in the second part of the duodenum which remains filled longer than normal, evidently due to adhesions.

CASE III.—Mr. H. K. E. is a business man of forty-six, who had typical hunger-pains for three years. I saw the patient first at the time of acute hemorrhage. A good-sized amount of blood was passed by the bowel and also vomited. A good result was obtained by the usual ulcer treatment in bed.

A Roentgen examination made two months later showed the characteristic deformity of the duodenal ulcer as seen in Fig. 246.

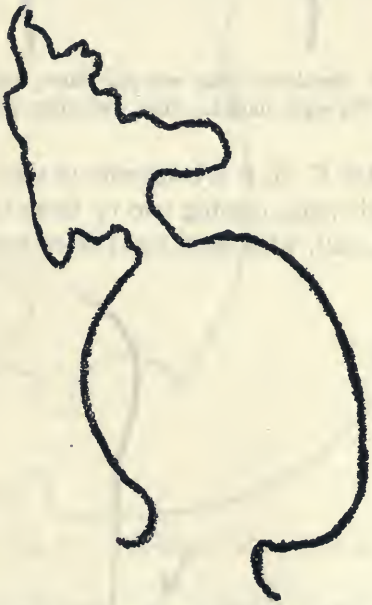

FIG. 246.—Case III. Duodenal ulcer, hemorrhage (life size).

The patient was a very nervous man and had many minor setbacks, but finally became free from digestive symptoms, and has remained so for nearly a year. Figure 247 shows the contour of the duodenum after eight months' absence of digestive symptoms. Instead of the marked deformity of the duodenum found at first with active ulcer, we have left a very small irregularity on one side of the duodenum, evidently a small area of scar tissue.

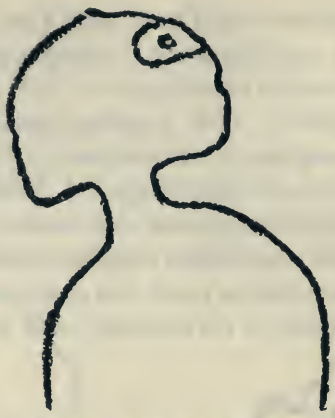

FIG. 247.—Case III. Duodenal ulcer, one year later, medical treatment free from symptoms for eight months, slight deformity persists (life size).

CASE IV.—Mrs. C. H. is a housewife of sixty-seven, who has had dull epigastric pain, coming two or three hours after meals for a year and a half, with little relief from soda or food. She

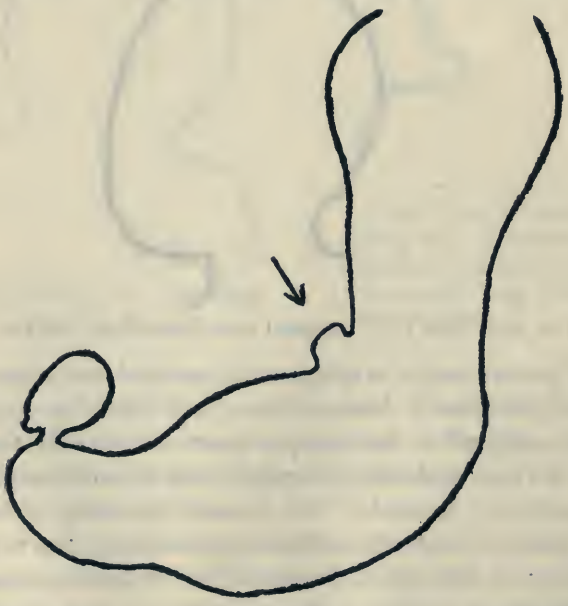

FIG. 248.—Case IV. Gastric ulcer of lesser curvature, operation refused.

has lost 5 pounds in weight. The stomach contents showed low normal secretion, without mucus, with a trace of blood with the benzidin test.

A Roentgen examination showed a stomach which emptied promptly; a characteristic ulcer crater about the middle of the lesser curvature, as seen in Fig. 248. The size of the ulcer crater was a little less than a 5-cent piece.

A diagnosis of gastric ulcer was made, with the possibility of cancerous degeneration and operation advised. The patient

FIG. 249.—Case IV. Six months later, no deformity seen.

refused operation and was put to bed and took the usual ulcer treatment. Her symptoms entirely disappeared. She gained in weight and has remained well for a year and a half.

A Roentgen examination of the stomach six months after beginning of treatment showed no sign of the ulcer at the lesser curvature or any other abnormality of the stomach (Fig. 249).

The next case illustrates a less complete result of medical treatment in a gastric ulcer high up on the lesser curvature.

CASE V.—Mrs. C. P. B., a housewife, aged fifty; formerly well; six months ago began to have sharp epigastric pain with-

out relation to meals, and vomiting soon after meals without blood, and lost 20 pounds in the last six months. Four months ago two cysts of the ovary were removed and a retroverted uterus pulled up into place. Following the operation the stomach behaved well until one month ago, when all the symptoms returned. She is a long, thin, frail looking woman, with a small tender area in the epigastrium. The stomach contents showed normal secretion; a trace of blood with the benzidin test.

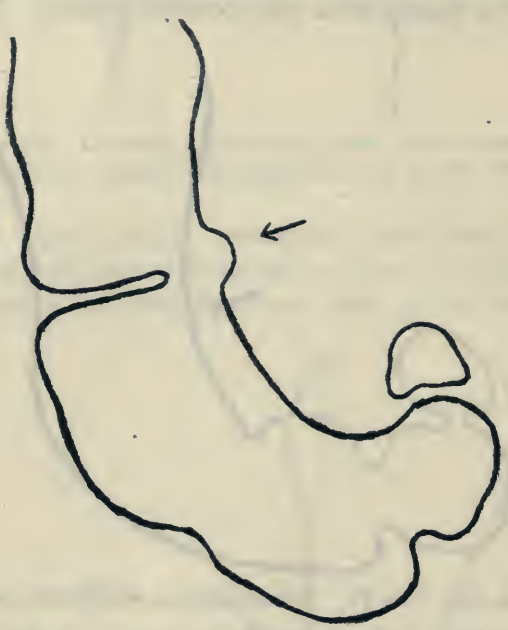

FIG. 250.—Case V. Gastric ulcer of lesser curvature, operation refused.

A Roentgen examination showed a characteristic ulcer deformity about the middle of the lesser curvature of the stomach. The crater of the ulcer was about 2 cm. wide and 1 cm. deep. There was a deep incisura of the greater curvature opposite the ulcer (Fig. 250). There was a good deal of ptosis of the stomach and bowel. The stomach emptied in six hours.

The diagnosis of chronic gastric ulcer was made, and she was put to bed and given the usual ulcer treatment. She gained steadily in every way until at the end of two months she was

free from symptoms and had gained 15 pounds. A Roentgen examination at that time (Fig. 251) showed that the crater of the ulcer is practically filled up smooth. There is a little incisura opposite the site of the ulcer which shows there is still some irritation there. On account of the general improvement and the anatomic change the prognosis was considered to be good. After this time the patient passed out from under my observation.

FIG. 251.—Case V. Two months later; no ulcer deformity, small incisura.

In Case VI we have an example of a duodenal ulcer not recovering under medical treatment, but being made fairly comfortable and refusing operation. The anatomic changes in the duodenum remain practically constant for months.

CASE VI.—Mr. A. T. K. is a manufacturer, aged forty; a hard worker; a rather nervous man; now retired for four years; had had many ulcerated teeth, none for a year; for fifteen years has had intermittent attacks of epigastric distress, coming one or two hours after meals, relieved by food or magnesia,

occasional severe vomiting; no blood; no old food; loss of about 8 pounds in weight.

Physical examination showed vague tenderness in the epigastrium; a moderate increase in gastric secretion, without blood or mucus.

Roentgen examination showed a stomach normal in position and outline, with deep vigorous peristalsis. There is a marked constant irregularity of the first portion of the duodenum

FIG. 252.—Case VI. Duodenal ulcer (life size).

FIG. 253.—Case VI. Six months later, medical treatment with partial relief of symptoms, operation refused, deformity persists (life size).

(Fig. 252). The appendix was seen, apparently normal. Examination of the gall-bladder was negative. A diagnosis of duodenal ulcer was made.

He was put on ambulatory ulcer treatment, with great relief of symptoms. There is a tendency for a slight disturbance to recur with indiscretion in diet, and it has been impossible to entirely clear up his disagreeable symptoms. He had gained 5 pounds in weight at the end of six months.

The second Roentgen examination six months after the first (Fig. 253) shows the deformity of the duodenum practically unchanged. In this case surgery was advised on account of the partial success of medical treatment, but the patient would not consider it.

Synopsis of Medical Treatment.—*Rest in Bed.*—This is needed for one to four weeks in the more severe cases, particularly the gastric ulcers, and all cases where there is much pain or such complications as obstruction, hemorrhage, or malnutrition. I always prefer a week in bed for all ulcer cases, but it is not absolutely necessary in the milder type of case, particularly the duodenal ulcer in vigorous men without complications. I have usually obtained excellent results in these cases by the use of diet and drugs without the necessity of taking the patient entirely away from his business and putting him to bed.

Local Applications.—A Preisnitz compress changed every twelve hours is frequently useful in relaxing spasm and making the patient comfortable. If there is pain, a flaxseed poultice may be used.

Diet is subject to more hobbies than any other part of the treatment; we must remember that radically different diet schemes in the hands of experts show very small variation in the percentage of cures. We have tried to make no restrictions that are not needed.

In the more serious cases we give two or three days of exclusive rectal feeding at the start, in order to rest and quiet the stomach, lower secretion, lessen peristalsis, relax spasm, and get the stomach entirely empty. We use 8 or 10 ounces of 10 per cent. glucose solution in water, to which 1 ounce of 50 per cent. alcohol may be added (Smithies). If necessary, 10 drops of tincture of opium may be put in every second or third enema. This is given by the drop method three or four times a day. Rectal feeding gives more water than food, but about 500 calories are absorbed, and the glucose prevents starvation acidosis.

When little or no food is given, chewing paraffin wax a half

dozen times a day keeps the mouth clean, stimulates the flow of alkaline saliva, and lessens hunger contractions and thirst.

We use chiefly carbohydrate foods at first because they cause little acid secretion and peristalsis. The pylorus is relaxed and opens easily. This keeps the stomach empty and the acids low. We use chiefly cereal gruels and cream soups or powdered crackers and milk. Milk is better given in cereal gruels or with egg, or predigested, or mixed with cream or crackers, on account of the tendency of plain milk to form hard curds in a sour stomach. The diet is a much modified Lenhartz. The following is the usual scheme:

First Week.—Strained cereal gruels or strained cream soups made from vegetables, or milk and cream equal parts, or powdered crackers and milk are given in hourly feedings, beginning with 1 ounce and increasing up to 3 or 4 ounces. If desired, the Lenhartz feeding may be given, namely, 8 ounces of milk and 2 eggs beaten up and divided into twelve feedings, one every hour. Each day add 1 more egg and 3 ounces of milk, until 6 eggs and 1 quart of milk are taken. On the third day add ½ ounce of sugar or milk-sugar to the beaten eggs, gradually increasing to 1 ounce of sugar.

Second Week.—One-half the eggs (3) may be soft cooked; three feedings of 1 ounce each of boiled rice or other well-cooked cereal (not oatmeal) served with sugar and cream. One-half to 1 ounce of butter per day. Gruels, cream soups, egg and milk, one or two pieces of very dry toast well chewed, or milk-toast, macaroni, Mellen's Food, or malted milk, custard, cream-toast, ice-cream. Six meals a day.

Third Week.—Add 1 or 2 ounces of scraped beef or tender chicken, chop or steak daily, also simple cornstarch, custard, and rice puddings.

Fourth Week.—Add well-cooked mashed vegetables; vegetable purées; apple sauce or stewed pear; finely chopped spinach.

After Fourth Week.—The foods to take are: milk; butter and cream soups; cocoa; soft cooked eggs in any form, two at a time, may be eaten as often as twice a day. Fish must be fresh and always broiled, baked, or boiled—never fried. Fresh beef,

lamb, mutton, or chicken may be eaten in moderate amounts once a day. The meats should be as tender as possible, always roasted or broiled, not cooked too much, cut fine on the plate, and well chewed before swallowing. Toast, crackers, breads, rolls, and plain cake when not too fresh are allowable at all of the meals, and plain fresh butter in large quantities. The cereals—cornmeal, hominy, cream of wheat, farina, rice—must be well cooked. The best vegetables are rice, mashed potatoes (white) or baked sweet potatoes, asparagus tips, young peas, chopped spinach. Any dessert made of cereals, butter, milk or cream can be used (custard, simple puddings), also simple jellies. Fruits—apple, pear, peach, prunes, apricots—should be baked or stewed. The best drink at meals is plain cool water or hot malted milk or cocoa.

General Directions.—Eat slowly, chew well; no very hot or very cold food; no worry at meals. Never eat until overfilled. Take a little lunch between meals, for example, a glass of malted milk or cocoa with one or two crackers. No raw fruits or vegetables for six months.

For the *ambulatory cases* we use the following scheme:

The general plan of the diet is three moderate-sized meals at regular intervals in the day, and supplemental meals of malted milk or milk reinforced with cream, cocoa, and crackers between meals and before retiring. All of the solid foods should be tender, cut very fine on the plate, and thoroughly masticated before swallowing. Altogether, foods should be taken at least five times in a day in one or the other of the two types of meals. No meat broths, condiments, spices, coffee, "soda water," alcohol, coarse or salted food, very hot or very cold foods.

The foods permitted for the main meals are cream soups. Eggs in any form about four in a day. Cereals (well cooked) with cream in the morning. Macaroni, vegetables, any that are well cooked and mashed, such as potato, squash, rice, finely chopped spinach (no green vegetables, fruits, berries or nuts). Desserts, any made of milk, eggs and cereals (custards, simple puddings), and jellies, cream cheese, cooked fruit—apple, pear, peach, prunes. The best drink at the meals is water, hot cocoa,

or malted milk. Butter, cream, milk, eggs, cereals, and bread remain the main foods of the diet. Olive oil should be taken after the main meals, a dessert or tablespoon.

After the first or second week fresh beef, lamb, or chicken roasted or broiled, or fresh fish broiled, baked, or boiled may be taken once a day.

The Stomach-tube.—This may be needed for the first few days *in cases with marked spastic obstruction* to help keep the stomach empty. There need be no hesitation in using it for this purpose in ulcer cases. I have never seen it do harm in a mechanical way.

In general, with atropin and a moderate use of alkalies, together with a bland diet and plenty of fats in small repeated feeding, the tube is not often needed.

If distress occurs in spite of very careful treatment, it is always fair to use the tube to see why (gastric stasis, overacid contents, etc.).

The Duodenal Tube.—I have given the duodenal tube a thorough trial in chronic ulcer, and no longer use it. It gives good results, I can vouch from my own experience, but I get just as good or better results by the treatment already outlined, with less discomfort to the patient. The duodenal tube has helped me more in cases of persistent vomiting in nervous women than in any other class of case.

Drugs.—The most useful are the alkalies and atropin.

Alkalies.—We give them on the theory that distress or pain is due partly to increased peristalsis and muscular spasm, and thus to delay in emptying the stomach and partly to irritation of the ulcer by free acid. Our object is to neutralize free acid and check spasm and help the stomach to empty. Nothing is more definite in medicine than the relief of hunger-pain in ulcer by alkalies. It probably is not necessary to neutralize every trace of free acid to get these good results. The use of excessive amounts of bicarbonate of soda may even irritate the stomach. Soda has been much discussed, and experts get excellent results in treating ulcer using either little or much, which shows that the amount given is not vital. I believe the middle

course is the best. Five to 10 grains of calcined magnesia is often better than bicarbonate of soda, whose neutralizing power is low, about one-quarter that of magnesia, and forms troublesome gas (CO_2). Many cases need no alkalies if the diet is properly regulated.

I believe that the scheme that Sippy has so much emphasized of giving small amounts of bicarbonate of soda and oxid of magnesia between meals at first is a good one. We may use milk of magnesia, 2 to 4 teaspoons, instead, and we can alternate the magnesia with a mixture of subcarbonate of bismuth, 10 grains, and sodium bicarbonate, 20 grains, if the bowels become loose. Some objection has been raised to this alkaline treatment on the ground of irritation of the stomach and hydrorrhea, but I find that this rarely occurs, and when it does appear, soon passes off.

The common fault of the family doctor in these cases is to use too little alkali, and to *wait till pain appears and then relieve it.* This is a serious mistake. It is very slow work healing an ulcer in this way. We should aim to *prevent the appearance* of these painful periods of spasm and peristalsis and acidity by frequent small feedings of bland food and by the use of alkalies *in advance of the customary periods of hunger-pain.* Patients are often "afraid soda will hurt the lining of the stomach," and need to be encouraged. A few patients with ulcer have habitually low gastric secretion; here alkalies are not needed.

Atropin, $\frac{1}{150}$ grain, two or three times a day, is very useful in relaxing spasm and checking secretion, and the bedtime dose is one of the best means of getting the patient comfortably through the longest interval between meals. I see no advantage in giving it subcutaneously except in cases of vomiting or hemorrhage, the physiologic result is so readily obtained by mouth.

Hydrogen peroxid promised well as a powerful means of checking gastric secretion, but it has proved too irritating, even when well diluted, and I have given up using it.

Bismuth is much used, and probably has some effect in protecting an ulcer. It is not important. In a series of test cases, giving every other case bismuth, no difference in the result was

noted. It is valuable as a corrective if much magnesia has to be used.

Tobacco.—If the patient is a smoker, it is very desirable to greatly reduce or omit tobacco.

Hemorrhage.—We want a quiet contracted stomach, to let the open blood-vessel retract and close the folds of mucous membrane and favor clotting. We want low or moderate blood-pressure. These indications are best met by a subcutaneous injection of $\frac{1}{4}$ grain of morphin with $\frac{1}{30}$ grain of strychnin, to keep the stomach contracted. Absolute rest in bed, no food by mouth for a few days, no vomiting, no unnecessary handling, no lavage, no rapid introduction of fluids, no stimulation unless the blood-pressure falls very low. We keep up the body warmth, and furnish some fluid by rectum or intravenously if absolutely necessary. A large enema of normal salt solution is usually undesirable. It fills the vessels, raises pressure, thins the blood, and lessens its coagulability.

In hemorrhage cases we always begin with rectal feeding alone, but have no hesitation in giving food by mouth after two or three days.

Lavage is dangerous and very undesirable, as a rule, on account of gagging, increase of blood-pressure, and peristalsis; cases are reported where the tube has helped by emptying a full bleeding stomach just as we empty a full uterus, but I have not seen one.

One of our first thoughts as we stand beside a bleeding ulcer patient is that we *must* stop the bleeding at once. Our second thought is that the various vasoconstrictors and coagulants are not very reliable. There are plenty of platelets and coagulating ferments in the blood, and little or nothing is gained by adding more.

We usually give $\frac{1}{2}$ to 1 teaspoon of a 1 : 1000 adrenalin solution in $\frac{1}{2}$ ounce of ice-water by mouth for local action in the stomach if the bleeding continues. It should not be used intravenously, as it promptly raises the blood-pressure.

With regard to coagulants, we know there is a natural steady increase in coagulability in hemorrhage. There is no lack of

any of the coagulation elements and the coagulation time is normal or less. Coagulants may be useful in small continued oozing or in preventing a second large hemorrhage, but the doses need to be given frequently, as their action is very brief.

There are many difficulties with blood-serums. The danger of severe anaphylaxis; they are not powerful coagulants; they rapidly deteriorate and are of little use after a week or two. It takes some hours to prepare serums freshly, and about a day passes after their subcutaneous use before they effect clotting. Fresh rabbit serum is the most useful, it is active and easy to get, and causes less anaphylaxis. It is given subcutaneously 10 to 50 c.c. every six to twelve hours for one to two days. The serum of stock diphtheria antitoxin has almost no value.

Coagulose made from horse-serum keeps for a long time and is active; 10 grains added to 8 c.c. of cold sterile water represents 10 c.c. of serum. It can be given subcutaneously, or into the muscle, or into the vein. It cannot be sterilized by heat. I always feel a little doubtful about the usual preparation, that is little called for and has been on the druggist's shelf for a long time.

Coagulen, a powder prepared from blood-platelets, is easily soluble in water and may be given by mouth for local action in the stomach in 1- to 3-ounce doses of a 10 per cent. solution in water. It is little used at present.

Calcium salts are hopeless in acute hemorrhage. They must be given in very large doses for many days.

The value of transfusion *in acute first hemorrhage* is under discussion, with the odds in favor of transfusion. This is more useful as a method of general help to a weak, anemic patient than as a method of stopping acute bleeding from an ulcer.

Surgery.—We always want medical treatment for *acute* hemorrhages from the stomach. It was only a few years ago when not a single patient in the two largest hospitals in Boston had survived an operation for acute hemorrhage from the stomach.

Nearly all acute ulcer hemorrhages stop under medical treatment and, as Moynihan says, not over 3 per cent. of freely bleeding ulcers could be saved by surgery at the time.

Recurrent hemorrhages, or oozing of blood which does not yield promptly to medical treatment, demand surgery. If such patients could be thoroughly examined, definite reasons for surgery could usually be found—large gastric ulcers, obstruction, etc. With the present intensive study which is made of chronic ulcer cases, very serious or fatal hemorrhages are becoming more and more rare. The serious cases are weeded out and dealt with more thoroughly and much earlier, and the risk of serious hemorrhage is greatly reduced. I have seen only one fatal hemorrhage from ulcer in the last seven years, and in this case there had been repeated warnings which, if attended to, I believe would entirely have prevented the fatal outcome. The persistence of occult blood for several weeks in spite of careful medical treatment makes one suspect cancer and justifies exploratory operation as a rule.

CLINIC OF DR. JAMES P. O'HARE

PETER BENT BRIGHAM HOSPITAL

CHRONIC NEPHRITIS WITH EDEMA

Report of a Case Terminating Fatally; Many Interesting Features, and Full Report of Autopsy.

IN this clinic I am going to discuss a case of chronic nephritis which has recently come to autopsy. The patient, a girl of ten, entered the Peter Bent Brigham Hospital August 31, 1917, and remained here continuously until her death on October 9, 1918—a period of more than thirteen months. During this time she has been under constant observation and study, as a result of which much useful data has been accumulated. Some of this can only be touched on here.

The past history of this little girl was unimportant except for an attack of "liver trouble" three years before entrance. This lasted for six months, was accompanied by jaundice, and kept her confined to bed almost all of that time. Now, this trouble may be of some significance as a possible cause of the onset of her nephritis, especialy since she gives an indefinite history of nocturia for one year. As you know, nocturia means awakening out of sleep to pass a goodly quantity of urine. It does not include voiding at night by a patient who cannot sleep. Accepting this definition then, nocturia is of considerable significance in determining the onset of any nephritis. Necessarily the nephritis antedates the appearance of this symptom. In our patient I have some doubt about the accuracy of the history of nocturia because during the patient's hospital career she rarely had this symptom.

The more probable etiologic factor in her was a rather mild

attack of diphtheria three months before coming to us. During this illness she was at the Boston City Hospital, and was discharged well. Incidentally, her family blames the antitoxin for the nephritis, whereas it was, of course, the diphtheria toxin.

Two weeks after leaving the city hospital her eyes became puffy. (Note that time—two weeks. The first symptom observed in most of our cases of acute nephritis is swelling of the eyes or feet, coming on ten days to two weeks after the patient is apparently well of the causative infection. The latter has usually been a throat or upper respiratory infection.) About one week later our patient noticed edema of the legs and—shortly—abdominal and facial swelling. No hematuria, headache, or drowsiness was noticed. She did, however, become nauseated and vomited a few times. She was compelled to go to bed, and two weeks before entrance 4 quarts of fluid were removed from her abdomen. She came to us for "swelling."

At entrance she showed general edema of the subcutaneous tissues reaching on the trunk as high as the manubrium sterni. The face was puffy, the legs were swollen, and there was considerable fluid in both pleural cavities and in the abdomen. The latter was tapped for relief almost at once.

Apart from the edema, physical examination showed but little. There was the characteristic pale, pasty expression to go with a somewhat lowered hemoglobin and an edematous face. Several teeth were necrotic. The tonsils were not at all enlarged. Bear in mind, however, that the small buried tonsils may be very much more dangerous than the large ones with plugged crypts.

The heart was of approximately normal size; the apex impulse being felt 9 cm. from midsternum, corresponding to the left border of dulness. The right border was percussed 3.5 cm. from midsternum. There was a soft systolic murmur at the apex. The radial arteries were apparently normal. The blood-pressure was 165 systolic, 95 diastolic. The urine showed a large trace of albumin, many granular casts, and a few red and white blood-cells.

Ophthalmoscopic examination made shortly after entrance showed no abnormality.

The picture, therefore, at this time was that of a subacute nephritis following diphtheria.

The patient's course in the hospital was essentially one of storing up fluid until she had to be tapped, and then refilling slowly again. As time went on the fluid accumulated less in her subcutaneous tissues and more in her abdominal cavity. In all, her abdomen had to be tapped fourteen times in fourteen months. There was nothing else in the course of her disease that was particularly unusual. She had an occasional headache and was easily nauseated and vomited. These symptoms, however, were usually prominent only when her abdomen was much distended with fluid. She was at all times rather weak. On the whole, it may be said that her hospital life was characterized chiefly by a series of abdominal taps.

In the last quarter of her stay with us her renal function tests had been showing a progressive decline. Two weeks before her death she had a slight but rising temperature. With this there developed an area on her cheek suggesting, very slightly, erysipelas. (I rather doubt that it was this disease.) At once her face became terribly swollen and the edema elsewhere increased rapidly. She voided less and less and was practically anuric for several days before death. In spite of this extreme oliguria the patient had but few symptoms. The urine picture changed to one indicating great degenerative changes in the kidney. The fields of the microscope were filled with casts of all kinds: hyaline, granular, and cellular. There was but little blood. The blood urea nitrogen had climbed rapidly to 90 mgm. and the phthalein excretion would undoubtedly have been zero if we could have made the test. (Output of urine was too low.) Toxic symptoms—severe headache, drowsiness, restlessness, urinous breath, terrible nausea, vomiting, and twitching—then appeared. Her heart became very rapid and irregular; she developed Cheyne-Stokes' respiration and died, retaining consciousness to the end. There was no evidence of any acidotic breathing and there was no acidosis. There were no convulsions.

Now, the outstanding interest in this case centers, of course, in the edema and the salt-and-water metabolism. Let us postpone this, however, until we have considered some of the other features.

The results of routine urinalysis were interesting. The specific gravity averaged about 1019 all along. This is pretty high concentration for such badly damaged kidneys as the pathologist found. Within ten days of her death she was able to concentrate to 1025 for a twenty-four-hour period. There was usually a slight trace to a trace of albumin, numerous hyaline, less numerous granular, and occasionally a few cellular casts. Red cells were numerous at first and gradually tended to disappear. White cells, which were also numerous, decreased more slowly. As has been stated before, during the last two weeks of life the kidneys were undergoing rapid degeneration. The urine, as a result, was loaded with casts of all kinds: hyaline, and the more significant coarse brown granular, and cellular casts. Curiously enough, there was but little blood.

Table I is a summary of the other features, and is taken from charts which are too cumbersome for this exercise. As you see, the patient's thirteen hospital months have been roughly divided into four equal parts. This is as good a division as any, inasmuch as there were no special episodes to make natural divisions. Let us consider some of the different items.

Take the blood-pressure first. On the whole, the diastolic paralleled closely the systolic, so that I shall consider only the latter. This pressure fluctuated moderately from day to day, with changes only indirectly connected with the disease. For example, there was a rise when the patient was up and about and a fall when she was put back to bed. There was also a slight rise when the patient's abdomen was much distended. Apart from such changes, however, the systolic curve is what you would expect. At entrance the pressure was moderately elevated, averaging about 160 during the first ten days. It then fell to around 135, where it remained for the greater part of a year. Now, remember that while a systolic pressure of 135 is

TABLE I

		First quarter.	Second quarter.	Third quarter.	Fourth quarter.	Maximum variations.
Blood-pressure, systolic	Maximum,	165	145	150	202	110–202
	Minimum,	111	120	125	110	
	Average,	135	135	135	150	
Blood-pressure, diastolic	Maximum,	100	110	115	130	70–115
	Minimum,	72	70	80	80	
	Average,	90	90	90	105	
Phthalein	Maximum,	43	55	38	34	9–55
	Minimum,	28	25	23	9	
	Average,	37	36	30	20	
Blood-urea, nitrogen[1]	Maximum,	77	27	41	122	11–122
	Minimum,	22	14	15	11	
	Average,	26	18	20	17	
Blood chlorid[2]	Maximum,	5.5	5.8	5.8	6.00	4.75–6.00
	Minimum,	4.8	5.6	4.75	4.85	
	Average,	5.2	5.35	5.25	5.50	
Urine volume	Maximum,	1375	650	1025	1400	0–1400
	Minimum,	100	150	150	0	
	Average,	400	300	300	750	
Urine chlorid[3]	Maximum,	0.54	1.1	0.56	2.88	0–2.88
	Minimum,	0.04	0	0	0	
	Average,	0.16	0.8	0.06	0.8	
Urine nitrogen[3]	Maximum,	12	4	10	8.8	0–12
	Minimum,	0.4	1.2	1	0	
	Average,	3	2	2	4	

[1] Mgm. per 100 c.c. [2] Grams per liter, whole blood.
[3] Grams per twenty-four hours.

normal for an adult, it is not so for a girl of ten. Her normal should be around 100.

During the last quarter there was a steady rise in pressure, reaching a maximum of 202 at about the onset of her final stage. This, of course, is very high, and is equivalent, in an adult, to something like 260. Such a pressure is unusual in a true diffuse chronic nephritic. It is more like what we see in the straight vascular hypertensive case. Curiously enough her blood-pressure fell in the terminal stage to 135 and then rose again to 175 two days before her death. This drop before death is not very

unusual and is probably due to a relaxation of the whole vascular system.

In general, therefore, it may be said that the blood-pressure was only moderately elevated during the greater part of the disease, was higher in the active stage at entrance, and extremely high a short time before death.

If you look at the excretion of phenolsulphonephthalein you will see that, on the whole, our patient did pretty well. During the first three-fourths of her hospital life the average excretion was 30 to 35 per cent. instead of the normal 60. Now this is not at all bad, and a glance at the maximum and minimum figures will show that at times the kidneys handled this dye-stuff almost as well as normally. At one time the patient excreted 55 per cent. in two hours and ten minutes. Bear in mind, however, that a pathologic kidney under no strain may show a normal phthalein excretion, but when the strain is applied the function may be much depressed. We have recently had a patient in the hospital who had a phthalein excretion of 45 per cent. and a normal blood urea and blood chlorid. He was operated on for his hematuria and a large polycystic kidney removed. There was not one bit of functionating renal tissue left. The other kidney was normal and was doing all the work. If you remove one kidney in a dog, the other will function normally under average conditions. Even in a diseased kidney the extent of the damage is not accurately gauged by the usual functional tests performed under conditions of comparative rest. In such a kidney the remaining good tubules and glomeruli hypertrophy and take on the burden of the damaged or destroyed ones. When these are pushed beyond their capacity, however, they give way, and the function, which has been good, becomes distinctly poor. The kidneys of our patient were doing a minimum of work and getting a maximum of rest on a low protein and low salt diet, etc.

In the last quarter there was a gradual but well-marked fall in the phthalein excretion—no doubt to zero if we could have performed the test at the end. Incidentally, it was during this period that the kidneys were put to the greatest strain by a

long period of high protein diets. I do not believe, however, that this could have had much influence on the phthalein excretion or on the outcome, since her kidneys, during this period of high feeding, did better work than at any other time in the disease. I refer to the excretion of water, salt, and nitrogen.

The blood urea nitrogen curve is of significance for three reasons: In the first place it was normal or nearly normal during the greater part of the disease. It shows conclusively that this substance may be normal when the function of the kidney in other respects is almost nil. For five weeks during which the phthalein excretion averaged 14 or 15 per cent. and even as low as 9 per cent., the blood urea nitrogen never went over 16 mgm. (15 mgm. per 100 c.c. is assumed to be the high limit of normality under average conditions). This points to the fact that the blood urea nitrogen is in itself not a sufficient test of renal function. When combined with the phthalein excretion we think it is quite so, even better than the more complicated Ambard or urea index.

In the second place this urea curve shows that this substance is dependent on the intake of nitrogen in the diet plus the breakdown of tissue protein. In our patient there were but three periods during which the blood urea nitrogen was much elevated. The first two correspond accurately to the taking of the high protein low fat diet of Epstein and the last, at the end of life, when there was a tremendous breakdown of body tissue. As a result of the latter there was a rapid rise in two to three weeks from normal to 122 mgm. per 100 c.c., *i. e.*, about ten times the normal.

A third thought is brought out in the comparison between the blood urea nitrogen and the phthalein curves. We are in the habit of assuming that as one falls the other rises. This is true in experimental acute nephritis in animals, and it seems to be true in many patients for a short time after they enter the hospital. With a low protein diet and rest in bed they begin to get rid of the excess nitrogen that they have been accumulating before entering the hospital. With this comes a relief of pressure on the kidneys and the function improves. In such a

case the phthalein will rise as the blood urea falls. There is really no relation between the two; at least in our case. The two were quite dissociated. With the fall in the phthalein from near normal to zero the urea in the blood remained at or near normal. Furthermore, in the episode of Epstein high-protein feeding, when the blood urea nitrogen rose the phthalein actually rose with it.

The urinary nitrogen curve is of no great significance, and there is but little excuse for doing this rather tiresome and monotonous grind. In this case the intake of nitrogen was low, the output was about normal. When the intake was raised the kidneys tried to follow. In this they were not very successful. On an intake of nitrogen of 3 to 4 gm. during the time when the patient was on a low protein diet, the kidneys excreted 2 to 3 gm. If you remember that 1 gm. or even more of nitrogen may be lost in the feces, you will see that the excretion of nitrogen by the kidneys was very good. When, however, the higher protein diets were fed the kidneys could not do as well. On an intake of 10 to 12 gm. they excreted only about 6 gm. It may be of interest to note that during the two Epstein diet episodes these kidneys were able to excrete as high as 10 to 12 gm. of nitrogen in twenty-four hours on occasions.

Now to consider the most interesting part: the salt-and-water metabolism. Let us take the blood chlorid. In most cases we feel that the determination of this substance reveals but little to us. This is due to the fact that the laws governing the concentration of salt in the blood are not at all established. Furthermore, it is known that certain drugs may change the concentration of this substance by displacement of it out of the blood-stream, presumably into the tissues. Outside the body, too, if one is doing the chlorids of the plasma, there may be an absorption of salt by the corpuscles if the blood is shaken too vigorously with air. The determination of the chlorids of the whole blood, rather than those of the plasma, obviates this last difficulty. In fact, it has been necessary for us to do this because we were unable to obtain blood charcoal.

In our case the blood chlorid was of considerable interest

in one or two ways. Its concentration was always somewhat elevated. The threshold of the kidneys for salt was undoubtedly raised. You know, of course, that the so-called "useful" substances in the blood, those like salt and glucose, which the body can keep on using, are supposed to have a threshold. When the concentration of these substances in the blood reaches a certain level they are no longer excreted in the urine. The "useless" substances, like urea, have no threshold, but are removed from the blood-stream as fast and as completely as the kidney can do so. Does it not seem extremely significant in our case that the chlorid was highest in the blood during the only time when the excretion of salt and water by the kidneys was good? This, too, was when the patient was taking a mixed diet high in protein, but low in salt. It would seem to point to the possible conclusion that the tissues were more at fault than the kidneys. It therefore seems fair to conclude that a combination of water and chlorid, perhaps with something else, occurred in the tissues, and that the feeding of the higher protein diets loosed this combination. Additional weight is given to this hypothesis by another experiment. While our patient was excreting but little salt and water we fed her considerable amounts of sugar in the form of candy. At times it seemed as though there resulted a short-lived increase in the excretion of salt and water. We are rather conservative about such interpretations, however, since we have found, all too often, changes in the excretion of different substances without any known cause. On occasions we have noted well-marked changes in the excretion of water, salt, and nitrogen on days when we had planned to carry out a certain procedure, but were prevented from so doing. You see how easy it is to misinterpret moderate changes.

Take next the urine volume. During the greater part of the hospital life she excreted a very small amount. On an average intake of 1000 c.c., the output equalled only 300 to 400 c.c. The difference was largely stored in her abdomen. There were three or four exceptional periods, however, during which the patient excreted a considerable amount of urine, in fact, had a diuresis. These periods were coincident with the giving of a diet high in

protein, either the Epstein diet or our own standard nephritic salt-poor diet. This is worth remembering, since we do not often think of giving our nephritics a high protein diet. Curiously enough, the Epstein diet increased the outflow of water, but did not affect the chlorid excretion. On the other hand, our mixed standard nephritic diet with a lower protein content produced a greater excretion of both salt and water. During less than a month of this diet, from July 26th to August 16th, the patient excreted 29 gm. of chlorid. This is only 9 gm. less than the entire chlorid excretion of the previous eleven months in the hospital. We had tried renal stimulants of all kinds, calcium lactate, purges, etc. but none of these had any appreciable effect on the water metabolism.

The chlorid output was as interesting as the water. We ordinarily think of these two as going hand in hand. But, as you have seen, it was not so in this case. The amount of salt excreted was extraordinarily small in comparison to the intake. The latter averaged about 2 gm. per day. In the table you will see that during the first nine months our patient excreted on the average not more than 0.1 gm. per day. In fact, there were many days (once five days in succession) when not a bit of chlorid could be obtained in the urine.

Where did this salt and water go? A glance at Table II will show you. This is a summary of the tappings, the volume of fluid withdrawn, the chlorid content of that fluid, the total urine chlorids excreted between tappings, and the approximate intake during these periods.

In ten months during which comparisons were made the patient took by mouth about 517 gm. of chlorid.[1] In that same period 418 gm. were recovered from the abdominal cavity, while only 98 gm. were excreted in the urine.

Just look at the column giving the figures for the volume of fluid removed from the abdomen. The patient was tapped in all fourteen times in as many months. If we include the fluid obtained at autopsy there was removed 96,500 c.c. This is

[1] See Table II, December 10th to September 27th.

TABLE II

Date of tappings	C.c. removed.	Cl. in fluid, gm.	Cl. intake, gm.	Cl. in urine, gm.
August 16th[1]	4,000			
September 1st	5,200			
October 1st	4,500		58	7.29
October 29th	5,700		56	6.54
November 13th	6,175		30	2.09
December 10th	4,800	32	56	3.66
January 10th	5,900	40	53	2.0
February 4th	6,200	41	48	1.7
March 7th	7,200	47	62	5.0
April 8th	6,785	43	64	5.0
May 2d	7,230	48	48	1.5
June 20th	10,000	69	60	3.0
July 17th	9,050	64	54	11.0
September 27th	8,260	54	72	65.0
Postmortem	5,500	24		
Total	96,500	462	661	113.78

[1] Before entrance to hospital; amount only approximate.

equal to well over 200 pounds, or three times the body weight of the child.

It may be of interest to know that the ascitic fluid in this case was always of the opalescent gray type, resembling, in its appearance, of course, chylous ascitic fluid. This sort of fluid has been typical of all of the nephritics we have seen in the last two years. In connection with the removal of the fluid in the abdomen the basal metabolism is of interest, too. It was found to be very low (—35) just before tapping. We thought that the removal of the abdominal fluid might raise this to nearly normal, on the assumption that the patient's true body weight —one of the figures used in the calculation—was more nearly correct after the removal of the fluid. This did not prove to be correct. The metabolism determined the morning after the fluid had been removed showed practically no change (—35 to —33).

The creatinin in the blood is supposed to be of assistance in determining the prognosis of a given case. This is based on the theory that this substance is handled with the greatest ease by the kidney. When, therefore, this begins to accumulate in the

blood it indicates that the kidney is badly affected. In our case it did not help us much. The blood creatinin was only 2.35 mgm. per 100 c.c. within twelve days of her death. With the rapid breakdown in tissue protein before death it rose rapidly, as one would expect, to 14 mgm. per 100 c.c.

Before speaking about the postmortem examination I should like to say a word about the eye-grounds in this case. These were examined repeatedly, and they seemed to be perfectly normal in every respect until the end. About ten days before she died she had blurring of her eyes, and examination showed moderate blurring of the optic disk in both eyes and a few spots of exudate in one eye.

We were indeed fortunate in getting an autopsy to complete this case. This, too, showed many interesting features. In the peritoneal cavity there were $5\frac{1}{2}$ liters of fluid. The omentum was much thickened, as was the peritoneum everywhere. This was brought out strikingly in the comparison between the serous surfaces covering the two sides of the diaphragm. The peritoneum was about three times as thick as the pleura opposite it. This is of interest because, you will remember, the fluid kept accumulating more and more in the peritoneal cavity. The pleural cavity was only occasionally affected. Whether this thickening of the peritoneum was responsible in great part for the deviation of most of the stored water and salt into this cavity or whether the thickening was secondary to the accumulation of fluid here is hard to determine. In this regard, the fact that the whole peritoneum seemed uniformly thickened and that those parts that were presumably most in contact with this fluid were no more thickened than the other may be of some importance.

The pericardial cavity contained a slight excess of fluid.

The heart was uniformly hypertrophied, and the chambers, especially the left, somewhat dilated. The valves were normal and the myocardium showed nothing except that the muscle-fibers were larger than one would expect for the age of our patient.

The aorta throughout its whole length together with its

main branches showed numerous yellow plaques of arteriosclerosis. The renal and splenic arteries were especially bad.

The spleen and liver showed chronic passive congestion. All of the other organs with the exception of the kidneys were normal.

These were very small, one weighing 95 gm. and the other only 65 gm. They were grayish-red in color, with smooth surface. The cortex was considerably thinned and there seemed to be considerable fat and fibrous tissue. On microscopic examination there was extensive fibrosis of the cortex and medulla. Many of the glomeruli were entirely replaced by fibrous tissue. The rest showed "all stages of intracapillary and capsular proliferation." There were none that were normal. The common lesion was a hyaline thrombus in the capillary with proliferation of the capsular epithelium. The tubules were tremendously atrophied. The arteries showed extensive lesions with many fresh thrombi and considerable sclerosis.

Summary.—In this clinic I have presented to you a case of chronic nephritis with edema, which came to us originally as a subacute nephritis following diphtheria. The patient showed a moderately elevated blood-pressure and at the very end a very high one. The renal function tests exhibited only moderate disturbances until near death, when the function became extremely poor. The chief interest in the case lies in the inability of our patient to handle water and salt. These two substances after a while were stored almost entirely in the abdominal cavity. Numerous tappings had to be performed for relief. The only periods during which our patient handled water and chlorid well were coincident with the feeding of a diet high in protein. No success was obtained in getting rid of a fluid during the periods of low protein salt-poor diets or, in fact, in any other way except tapping.

Postmortem showed a marked glomerular nephritis, hypertrophied heart, and extensive arteriosclerosis.

CLINIC OF DR. FRANCIS W. PEABODY

Peter Bent Brigham Hospital

SOME LESSONS OF THE WAR IN THE FIELD OF CARDIAC DISEASE

The experiences of medical men during the war have thrown much light on the subject of cardiac disease, and the knowledge gained is of value not only in the handling of soldiers but also in the care of civilian patients. It seems worth while, therefore, to call attention to some of the points which have been learned and to some of the problems that have arisen, so that we may carry back into our civil practice as much as possible of what we have learned during our service in the army. The patients to be discussed at this clinic are all discharged soldiers. The first illustrates the functional efficiency of certain well-marked cases of valvular heart disease. The second is to call attention to a stage of valvular heart disease rarely seen in civil practice, and to show the difficulty of diganosis in early mitral insufficiency. The third is to show a condition bearing superficial resemblance to heart disease and now generally known as the "effort syndrome" or the "irritable heart of soldiers." It is a type of case which became particularly prominent during the war, but which exists potentially, and often unrecognized, in civil life. Certain types of this condition are the direct product of the stress and strain of war, but in our army most cases have shown symptoms which antedated the mobilization by many years.

Owing to the careful and for the most part skilful work of the Cardiovascular Boards which examined the recruits only a very few men with valvular heart disease were accepted for service. Those who slipped by were, for the most part, men

without symptoms, and in whom the signs were obscure and difficult to recognize. It is indeed remarkable that, considering the haste and the difficult circumstances under which the examinations were carried on, so small a number of mistakes were made. Nevertheless a few men with heart disease were accepted. It is, however, probable that most of these were passed in the early weeks of the recruiting, before the examinations reached the high state of efficiency to which they finally attained.

CASE I.—The young man whom I wish to present to you first was invalided home from France in the summer of 1918, and was sent to the General Hospital at which I was on duty. He presented himself to me one day and reminded me that four years ago he had been a patient in my ward at the Peter Bent Brigham Hospital in Boston. He told me that he had been in the hospital on account of heart disease. Briefly his history in the army had been as follows: He had volunteered in the fall of 1917, had been hastily examined, accepted, and sent to France. There he had undergone strenuous training until he was sent to the front, where he "carried on," doing full duty without any difficulty for five months. During this time he hiked with full equipment. When asked as to the strain under which his heart gave out, he said: "My heart didn't give out at all. I got gassed. Then I was sent to a hospital, where they found a murmur and sent me home." His general condition bore out his story, for he was in excellent shape, and was able to take the severest of the graduated exercises without any difficulty. Let us now consider for a moment his past history. I turn to the record made in September, 1914, at the Peter Brigham Hospital, when he was fourteen years of age. The diagnosis at that time was "rheumatic fever; chronic cardiac valvular disease; aortic regurgitation; mitral regurgitation, and delayed conduction time." The previous history was as follows: In 1909 he was in bed for three months with an attack of rheumatic fever in which nearly all of his joints were involved. The following year he had a recurrence of the rheumatism which again involved all his joints and kept him in bed for four months. The next year he had a third attack of rheumatic fever, after

which he noticed that he became short of breath rather easily. In the summer of 1913 he had a fourth attack, in which, however, only one ankle was affected. After this he was up and about and was not bothered by any marked shortness of breath. The illness for which he entered the hospital began early in September, 1914, with a sore throat. Following this his ankles became swollen and stiff and it hurt him to walk. He did not feel feverish until the day before admission and he kept up and about until then. On the day before admission he began to have pain in the left side of his chest and some dyspnea. During the night he was unable to sleep lying flat. On physical examination he was found to be moderately dyspneic and very slightly cyanotic. The heart's action was regular and moderately rapid. The apex impulse was felt in the fifth interspace 12 cm. to the left of the midsternal line, and the cardiac dulness extended from 3 cm. to the right of the midsternal line to 13 cm. to the left in the fifth space. At the apex the first sound was followed by a long blowing systolic murmur which was transmitted toward the axilla. In the aortic area no second sound was audible, but there was a rough systolic murmur transmitted into the vessels of the neck, and a diastolic murmur which was loudest in the third interspace to the left of the sternum. The lungs were clear and the abdomen negative. The liver was not enlarged. There was a moderate amount of edema over both tibiæ. The electrocardiograms showed a prolonged conduction time. The blood-pressure was 120 systolic and 46 diastolic. During the first part of his stay in the hospital he had a moderate degree of fever, but his temperature soon reached normal, and with rest in bed and a little digitalis his heart became fully compensated. He was in the hospital for over two months, and on the last note before his discharge the border of the heart was made out to be 12 cm. to the left of the midsternal line in the fifth space. The electrocardiograms showed that the conduction time had become normal in length. At the time of his discharge he had little dyspnea or rise of pulse-rate when walking about the ward. He had made an excellent recovery, and left the hospital in good general condition.

Here, then, was a boy with a history of multiple attacks of acute rheumatic fever which had left him with a heart markedly enlarged and with perfectly evident signs of aortic and mitral insufficiency. He was hardly the material out of which one would expect to make a good soldier, and it is, of course, rather extraordinary that he was able to pass the physical examination of the army. On his return to Boston, after being discharged from the army, he again reported at the Brigham Hospital. At this time the area of cardiac dulness extended from 2.5 cm. to the right of the midsternal line to 14 cm. to the left. At the apex there was a distinct systolic and a diastolic murmur, and both of these became louder over the base of the heart and along the left sternal margin. It is possible, therefore, that his heart is now slightly larger than it was on his admission to the hospital, but this is not definitely so, for on various occasions during his stay in the hospital the left border was made out to be 13 to 14 cm. to the left of the median line. There is no essential change in the character of the murmurs and, indeed, it is difficult to say that there has been any change in physical signs of the heart since he was discharged from the hospital. With regard to the development of symptoms, he says that he never noticed any shortness of breath until the time he was gassed. Since that time he states that he has been moderately short of breath on exertion. We know, however, that this is not an uncommon result of gassing, and it would hardly be a fair conclusion to regard this as necessarily being a symptom of his heart disease.

One would hardly propose that the physical and nervous stress of war should be used as a functional test for patients with cardiac disease, but in this case the result of an accidental experiment has proved extraordinarily interesting. From the physical examination of his heart few of us would have considered it possible that he could have undergone the strain of the last months. Not many physicians would have been bold enough to advise strenuous exercise for a young man with so large a heart and with aortic and mitral valvular lesions. Indeed, if he had placed himself under a physician's care he would probably, and very properly, have found himself leading a limited

existence. As it is, he has demonstrated again the teachings on which Sir James Mackenzie has so often laid stress. The examination of the heart, and especially the presence of cardiac murmurs, should be regarded as *in themselves* comparatively unimportant matters. The important thing is what the patient can do, and this depends largely on the quality of the heart muscle. Given as strong a heart muscle as this man must necessarily have, and he can compensate for a considerable valvular lesion. A heart with an injured valve works, it is true, at a considerable disadvantage, and its reserve power is usually reduced, but if the muscle is strong and healthy the heart may still do efficient service as long as the valvular lesion is not too extreme. To give a proper prognosis, therefore, we ought to have some knowledge of the condition of the heart muscle. Unfortunately, this is where our methods of physical diagnosis are inadequate. We can determine the condition of the valves with comparative accuracy from our objective examination, but this tells us little about the quality of the myocardium. We still wait for a satisfactory functional test of the heart, and in the meanwhile the best test is to try the heart out under the test of gradually increasing exercise, and see what it can do. Here, then, there is also indicated the path which should be followed in the treatment of the chronic stages of valvular heart disease. The first indication, it appears to me, is to prevent, as far as possible, the occurrence of subsequent infections which may cause further damage to the heart valves and further injury to the heart muscle. The second indication is to increase, as much as possible, the strength of the heart muscle. The problem of increasing the strength of the heart muscle is very similar to the problem of increasing strength of skeletal muscles. Both are improved by properly supervised exercise, which does not reach the point of fatigue. It is an error to believe that all persons with valvular heart disease should lead an extremely limited existence. Too much rest may only result in the production of a weak, flabby heart muscle. Proper exercise will result in the strengthening of the heart muscle so that it may more easily overcome the disability which it suffers from having

injured valves. It is important, of course, that exercise should be somewhat supervised and should not be overdone, for fatigue is of no benefit to cardiac or to skeletal muscle. In general, the best indication as to whether any given exercise is appropriate or not is whether it produces dyspnea, or pain, or palpitation. If exercise causes no distress, it is probably not harmful. Of course, in any given case, it may take some courage on the part of the physician to start his patient on exercise. Much more courage, however, is often needed by the patient, who has usually had it enforced on him that he must be extremely careful about the amount of physical exercise that he takes. If, however, one uses common sense as the guiding principle, the results will rarely be other than beneficial, and the natural outcome is that the cardiac condition will improve as the patient gets into better general training.

The experience which the patient before you has had is by no means unique, and it has been very striking to see how many men with valvular heart disease have stood up under unusual strain in the army. I have personally seen a considerable group of cases of definite aortic insufficiency who have carried on full duty without developing any symptoms, and who have apparently been none the worse off for their experience. The diagnosis was made in these patients as the result of their coming into the hospital for some reason other than heart disease. Many soldiers have, of course, had their hearts give out while in the service, but the majority of these have been older men with myocardial weakness and men with syphilitic lesions. Mitral stenosis, too, seems to have a poorer prognosis than mitral or aortic insufficiency. Not every case can carry on as successfully as the patient just presented to you, but it has been very striking to see how much reserve force the heart may have in a young man with valvular heart disease of rheumatic origin, provided he is otherwise healthy. It is, I think, a profitable lesson for us all to see what these men can stand up under, and it will give us faith that many of our patients in civilian life can probably do a good deal more than most of us would have been inclined to give them credit for. While no one would

knowingly submit such men to the strain which they have been under in the war, many of them seem to have come through without doing themselves any harm.

CASE II.—This patient is twenty-four years old, and before he entered the army he was at work as a clerk. At the age of eighteen he had an attack of rheumatic fever involving the elbows, wrists, and knees. He made a good recovery and was never told that his heart was at all affected. Since that time he has been perfectly well and has been working regularly. He takes a moderate amount of exercise and has never had any symptoms which were referable to his heart. At the beginning of the war he volunteered, but was told by the examiner that he had a "murmur in his heart" and was refused enlistment. Later, however, he was drafted, accepted by the examining board, and sent to one of the large camps. From there he was sent overseas in the spring of 1918, and while in France he "carried on," doing full duty in one of the training areas. After two months he had an attack of acute tonsillitis, and shortly after the onset of this, his right ankle became swollen, red, and tender. He was sent to a hospital, and during his convalescence a doctor again found a murmur on examination of his heart. A diagnosis of valvular heart disease was made and he was transferred through several other hospitals until he was sent back to America. He says that during his stay in the different hospitals there were at several times discussions about his case, and much doubt was expressed by various physicians as to whether or not he had a valvular lesion. He has recently been discharged from the army, and now comes to the hospital for an opinion as to the exact condition of his heart. Subjectively, he apparently feels perfectly well. When questioned directly as to the occurrence of dyspnea, he says that he sometimes gets a little short of breath on climbing two flights of stairs or on going up a comparatively steep hill, but he has been in hospitals for a long time and he thinks that this shortness of breath is accounted for by his being generally "soft." He has had no precordial pain. In appearance he is, as you see, a strong, healthy looking young man and his general physical examina-

tion is entirely negative. Let us now turn to the examination of his heart. The apex impulse is in the left nipple line. The impulse is not unduly forcible and no thrills are felt on palpation over the heart. On percussion, the left border of cardiac dulness is just outside the nipple line, and the right border is 1 cm. to the right of the sternal margin. The action is regular and the heart's rate 80 per minute. On auscultation with the patient standing up the first sound at the apex is of good quality and followed by a soft blowing systolic murmur. This is transmitted a short distance toward the axilla. There is no accentuation of either second sound at the base, but the pulmonic second is somewhat louder than the aortic. On complete expiration there is a rather loud systolic murmur in the second intercostal space just to the left of the sternum. When he lies down the systolic murmur at the apex becomes much louder, and over a small area at the point of maximum impulse the murmur replaces the first sound entirely. The distribution of the murmur is considerably wider when he is lying than when he is standing. The systolic blood-pressure is 125 mm. and the diastolic is 80 mm.

The problem in differential diagnosis before us is to decide whether this is a normal heart or whether the patient has mitral insufficiency. In settling this question, the points in the physical examination to which we must pay particular attention are the size of the heart and the presence of the murmurs. On percussion, the left border of the heart is about 1 cm. outside of the generally accepted normal standard. From this one might be inclined to assume that there is a slight hypertrophy, but, on the other hand, such a percussion outline has been found to be not uncommon in soldiers who are on active duty, and in the early part of the war careful *x*-ray studies of the hearts of soldiers doing heavy duty in foreign armies showed that slight enlargement was frequently present. The *x*-ray examination in this case shows that the size of the heart is about at the upper normal limits, and that there is no definite enlargement. The electrocardiogram is perfectly normal and gives us no indication of hypertrophy. In spite, therefore, of the somewhat unusually

wide area of percussion dulness we cannot assume that the heart is definitely enlarged.

Now as to the murmurs. The systolic murmur in the pulmonic area, in the second space just to the left of the sternum, is easily disposed of. It disappears on deep inspiration, but becomes very loud on full inspiration. This is a type of murmur that is very common in normal hearts, and especially in children and in young men and women, but it has been the basis of much discussion in the literature, and the fact that it is not pathologically significant does not seem to be generally appreciated. The exact mechanism by which it is produced is not definitely known, but it seems probable that the disappearance of the murmur on inspiration is due to the fact that the edge of the upper lobe of the left lung becomes interposed between the pulmonary artery and the sternum. Its appearance on full expiration is accounted for by the retraction of the edge of the lung and by the direct pressure of the ribs and sternum on the pulmonary artery. That the occurrence of the murmur is due to pressure on the artery is furthermore suggested by the fact that the murmur is most commonly heard in persons in whom the upper part of the chest is flattened.

The other murmur in this case occurs at the apex in systole and has a blowing character. It is well heard in the erect position, but when the patient lies down on his back it becomes much louder and it is transmitted toward the axilla. In character it is exactly similar to the murmur heard in typical mitral insufficiency. On the other hand, it also resembles very closely the accidental murmurs which are so often heard at the apex of the heart, and of which so much has been said in connection with the examination of soldiers. It is largely since we have been examining such great numbers of normal people that we have begun to find out in how large a percentage of healthy men systolic murmurs may be heard. Owing to a lack of appreciation of this fact the diagnosis of valvular heart disease has undoubtedly been made in a great many instances in which it was unjustified, and it is probable that many men have been kept out of the army for wholly unnecessary cause. The same

problem was apparently met with in England at the beginning of the war, and such authorities as Sir James Mackenzie and Thomas Lewis have laid great stress on the importance of recognizing these accidental murmurs. Indeed, the general feeling of most experts on cardiac diagnosis at the present time is that one should pay very little attention to a systolic murmur in itself, regardless of what its character, transmission, or loudness may be. The importance of a systolic murmur will depend largely on the other features of the cardiac and general examination. Thus, a systolic murmur occurring at the apex in a heart which is otherwise normal should be regarded as having no pathologic significance. On the other hand, a systolic murmur at the apex in association with definite cardiac hypertrophy is of much importance in making the diagnosis of mitral insufficiency.

We have, then, a heart which is not definitely enlarged, and we have a systolic murmur at the apex to which we are agreed importance can only be attached if it is found in association with other evidences of disease. Are we, therefore, to conclude that this heart is perfectly normal and give the patient a clean bill of health? I should be inclined to do so without much hesitation were it not for one important fact in the history. This patient had a typical attack of rheumatic fever at the age of eighteen, and a few months ago he had what appears to have been a second, milder attack. Since we know how very frequently the heart valves and the heart muscles are affected by acute rheumatic fever, it would seem that this point in the history must be regarded with seriousness. In cases of mitral insufficiency, as we usually see them in practice and in general hospitals, the diagnosis is not usually particularly difficult. There is almost always a well-marked hypertrophy of the heart, and frequently a definite accentuation of the pulmonic second sound in addition to the characteristic murmur. The significance of the accentuation of the second sound in the second left intercostal space is often overestimated, for the second sounds at the base vary greatly in intensity in normal persons and with change in position, and also because the sound heard in the so-called "pulmonic area" is often chiefly the aortic sec-

ond sound. Besides these physical signs, however, the patient usually complains of such symptoms as pain in the chest or dyspnea. These are well-marked, clear-cut cases who have usually reported to the physician on account of troublesome symptoms. By the time the symptoms have arisen the diagnosis is usually comparatively easy. We are then dealing with a rather advanced stage of the disease. Is it not probable that there is an earlier stage of the disease in which the diagnosis is much more difficult? This patient—and he represents a large group of men presenting the same problem in the army—did not come to the hospital on account of any symptoms. He feels perfectly well. Is it not quite possible that he represents an earlier stage of the disease than we are accustomed to see? May this not be a stage in which the heart is perfectly well compensated without demonstrable hypertrophy? In the usual course of his life he would never have thought of consulting a doctor at this time, and the findings in his case are to be regarded as practically accidental. If this be the case, then mitral insufficiency, which is usually regarded as being an easy diagnosis to make, becomes an extraordinarily difficult diagnostic problem. It seems to me that one cannot settle the question wholly on the basis of the physical examination. To do so might do the patient a great injustice. The history of attacks of acute rheumatic fever, which are so apt to cause damage to the heart, is too important a factor to be neglected. It would seem to me, therefore, that in a case with this history and with these signs one must incline to consider that we are dealing with an early stage of valvular heart disease.

Having made this tentative diagnosis, one must then be very careful as to the advice which he gives to the patient. The first important point in the treatment of the chronic stage of valvular heart disease of rheumatic origin is to do all that is possible to prevent any further damage to the heart as the result of more acute infections. One should consider the advisability of removing his tonsils, which are rather large, and thus possibly obviate any further attack of rheumatic fever, in case the portal of entry should be the tonsils. We should also caution him as

to the danger of exposure to cold and wet, for it is quite clear that persons who have had rheumatic fever once are more liable to subsequent attacks. It is also fair to tell him that the more frequent attacks of rheumatic fever a person has, the more liable he is to have serious damage done to his heart. The second important point is with regard to the general character of his life. One is often tempted, in such a case, to lay undue stress on the dangers of exercise and overexertion, and to make of him a semi-invalid, whose life centers about his heart. By so doing he is made to lose much of the normal happiness and satisfaction of life, and no adequate benefit is derived as far as his heart is concerned. It is much better to impress on him the fact that he ought to forget his heart and consider only his general physical condition. That which puts him in the best physical training is probably the best thing for his heart. He should be encouraged to lead a healthy normal life, and to take regularly such exercise as he can without any discomfort. He should avoid overdoing, but on the ground that marked fatigue is harmful to the organism as a whole rather than because of its effect on the heart. Beyond this he should be allowed to live a normal life. One should tell him that he has some slight affection of his heart, that it is important for him to return every year to have his heart examined, and that he should report to the doctor if at any time he begins to notice symptoms. He should also be told that he had better come for advice if he plans to undertake any extraordinary amount of exertion, but apart from this he should be told to go ahead and lead a perfectly normal life. For ourselves, as physicians, the important lesson to be learned from this case is that we are confronted with a problem which we cannot definitely solve. On the basis of our physical examination alone we cannot state whether this man's heart has been affected or not. Knowing his history, we must act conservatively, and then we must follow this and other similar cases over long periods of years until we are finally able to determine whether or not there has been any cardiac lesion. When these cases, which have come into our hands in an accidental manner, shall have been followed carefully for long periods,

we shall be in a position to make much more definite statements as to the problem of the early diagnosis of mitral insufficiency.

CASE III.—This patient is an unmarried man of twenty-seven years, who has come to the hospital for an opinion as to the condition of his heart. He says that some years before entering the army he was told that he had "heart disease," but that while he was in the army various doctors told him that this was not the case. His history is as follows: His father has always been a perfectly healthy man, but his mother is extremely nervous and has been so as long as he can remember. He is the youngest of three children, and has one sister who is nervous in the same way that his mother is. As a child he had measles and chickenpox. He has had no other serious diseases, but has never been strong and vigorous. At the age of fourteen, after a short febrile illness, the nature of which he does not know, he was taken to see the doctor, who told him that he had a "weak heart." The only advice given to him was that he must be "very careful." Since that time, he says, he has taken "the best of care of himself." His mother has worried about him a good deal, and has protected him in every eay. He has never been allowed to overexercise. This restricted life has, however, been no particular hardship to him, for he never cared much for active games. Even as a child when he tried to play baseball he used to get tired and out of breath easily. He graduated from high school and then went to work as a clerk in a store. His first job was in a large busy establishment, where the strain was rather heavy, and he found he could not stand it, so he sought out an easier position in a quiet place, where the nervous strain was much less intense. In this new position he has done well, but he gets tired very easily. He rarely loses any time from his work, but he has to be very careful not to overdo. He takes the cars to and from his work and stays at home in the evening. He says he does not exercise, and inquiry reveals the fact that he probably does not walk a mile a day. When he does walk he moves slowly, for he finds that if he hurries he gets tired and out of breath. He is at times troubled with

palpitation, and this may occur without apparent cause at night. He is extremely nervous and is easily upset if any little thing goes wrong. He has occasional headaches. He has found that he cannot stand any unusual nervous or physical strain, and for this reason he has tended to cut down his activities from year to year. In the summer of 1918 he was drafted into the army, and, to his astonishment, he was accepted as a soldier. This surprised him very much, for he says he had always known he had a weak heart. He was started in drilling at the camp, but found much difficulty with it, and says that even on the first days, when the work was light, he became extremely exhausted by it. He noticed palpitation, and then began to feel pain over his heart. When this occurred, he reported to the doctor, but was told that there was nothing serious the matter with him, and that he had better go on with the work. It is rather noteworthy that the amount of physical exercise of the drills at this time was slight, and on direct questioning he states that he was made very nervous by the attitude of the non-commissioned officer. He was much worried by the rigid discipline, and was fearful lest he should do something that would lead his superiors to find fault with him. He was sent one day to the rifle range, but when the firing began he shook so much that the officer took his gun away from him. He says that the shooting "unnerved him." On the way home from the rifle range he felt exhausted and the pain over his heart became intense. He fell out of line on account of shortness of breath, and he says that his heart was beating very fast. He was put into an ambulance and sent to the hospital, where he was kept in a ward until he was discharged, just after the armistice was signed.

On physical examination, you see, he is a fairly well-nourished, rather underdeveloped, nervous looking individual. The color of his lips is good, but both hands are cold, clammy, and cyanotic. When he extends his fingers there is a marked coarse tremor. They thyroid gland is somewhat enlarged and soft. There are no thrills or bruits over it. The general physical examination is entirely negative except for the fact that his reflexes are some-

what hyperactive. The rate of the heart as he stands before you is 125 per minute. The systolic blood-pressure is 140, and the diastolic 90. The apex-beat is very forcible and covers a wide expanse, being seen in several intercostal spaces. There is a slight thrill at the apex, which is apparently systolic in time. On pressure over the apex and in its vicinity, there is definite tenderness. The left border of cardiac dulness by percussion is in the left nipple line, and there is no enlargement of the heart to the right of the sternum. In the erect posture the first sound is loud, and there precedes it a slight roughening suggestive of the presystolic murmur of mitral stenosis. At the base both second sounds are loud. On lying down, the heart is slower. The first sound is less loud and the presystolic roughening has largely disappeared. At the apex a soft blowing systolic murmur is audible. The pulmonic second is somewhat louder than the aortic second. The electrocardiogram is normal and the *x*-ray shows that the heart is not enlarged.

Let us now consider the interpretation of the physical signs. The systolic murmur at the apex, which is brought out by lying down, is quite typical of the common accidental murmurs, and has in itself no significance. There is no hypertrophy of the heart, and there is nothing in the past history to lead us to suspect that there might be a valvular lesion. The presystolic roughening heard in the erect position is of interest because it is a common phenomenon which led to much confusion in the examination of recruits in whom it was often supposed to be evidence of mitral stenosis. It differs, however, from the murmur of mitral stenosis in several ways. It is shorter in duration than the typical murmur of mitral stenosis. It is usually heard in a rapidly acting heart, while in typical mitral stenosis the heart is apt to be slower, unless there is some other complicating factor. The thrill associated with it is systolic in time, and not presystolic, as in mitral stenosis. This murmur is usually best heard in the erect posture, and disappears on lying down, while the murmur of mitral stenosis is more apparent in the recumbent position. The disappearance of the murmur on lying down, when the heart falls away from the chest wall, suggests that the

murmur may be extracardiac in origin. It has been shown by Morison[1] that the two murmurs can be differentiated by an inhalation of amyl nitrite, if one auscults during the period of rapid heart action. Following the inhalation one finds that the murmur of mitral stenosis becomes louder, while this spurious murmur disappears. There is, indeed, a certain resemblance between this murmur and that of mitral stenosis, but if one bears in mind that this type of sound is common in the overacting hearts of nervous people with thin chest walls, there should be little difficulty in distinguishing the condition. In the absence of any hypertrophy, then, and in the absence of a history of rheumatic fever, we can safely exclude the presence of valvular heart disease in this case. We must consider the possibility of the tachycardia being due to Graves' disease, and in many similar cases in the army this diagnosis has been made. He has, it is true, a somewhat enlarged thyroid gland, and he comes from the region of the Great Lakes, where it is well known that goiter is endemic. The thyroid gland is, however, not larger than is frequently found in young adults, and it is softer than is commonly the case in Graves' disease. Moreover, it has been found that if he lies down quietly for an hour or so his pulse-rate drops to 80. This is an important point in the differentiation, for in Graves' disease the pulse does not usually show such complete slowing with rest. A good deal of investigation has been made into the problem as to whether cases similar to this depend on overactivity of the thyroid gland. In England Dr. Thomas Lewis found that the administration of thyroid extract did not increase the symptoms, and in this country, at General Hospital No. 9, in Lakewood, New Jersey, it was found that the basal metabolism is normal. The evidence is, therefore, entirely against the fact that the thyroid gland bears any relation to this condition. Clinically, also, the patients are of a different type, for while they are often extremely nervous, they lack the characteristic energy and "drive" of the typical hyperthyroid subject. It is usually extremely difficult to make a soldier with Graves' disease undergo a rest cure in bed, but I feel quite cer-

[1] Morison, J. A., Brit. Med. Jour., i, 1918, 452.

tain that we should not have any difficulty in enforcing such a quiet, dull régime on this man.

This patient presents the combination of nervous and physical symptoms, which are typical of the condition generally known as the "irritable heart of soldiers" or "effort syndrome." A tendency to fatigue easily is perhaps the most characteristic feature of the picture. With this one finds dyspnea on slight exertion, and palpitation and precordial pain coming on even when at rest. A rapid pulse, a coarse tremor, involving the fingers, hands, arms, and sometimes the legs, cyanosis of the extremities, and marked sweating are common accompaniments. Associated with this, and often overshadowing everything, is a very neurotic temperament. On account of the large number of recruits presenting this clinical complex, the condition became one of great importance in the army, but it is also a condition which is very common in civil life. One may recognize in general two distinct types. In the first place, there are those in whom the symptoms are of relatively short duration. In these men the symptoms have arisen in the army, and they are directly or indirectly the products of army life. The commonest etiologic factors seem to be infection, gassing, and the nervous and physical strain of warfare. In many instances the patients in this category are analogus to those in whom the diagnosis of "shell-shock" is made, and, indeed, many of these men are sent to neurologic hospitals. It often seems to be purely a matter of chance as to whether they are sent to a cardiac ward or a neurologic ward. Cases similar to these, in which the symptoms can be traced to some psychic trauma, are also seen in civil life, but they are less frequent than the second group of patients. In this second group the symptoms are of long standing and often date back to childhood. It is of this type that the patient before you is an example. In them inheritance may play a rôle, for it is not uncommon to find some nervous factors in the family history. The subjects of this group cannot be regarded as being directly the product of the war. Their symptoms have existed for many years before they entered the army, but they were able to limit the production of their symp-

toms by living below the level of nervous and physical strain which brings them out. This was the commonest type of "effort syndrome" seen in our army, but it is probable that if the war had continued longer, and our men had been forced to go through the severe strains endured by our Allies, we should have had many more of the acute cases. Before entering the army these men have usually been regarded as underdeveloped normals, or perhaps they have been classed as neurasthenics. In general, they have got along pretty well because they have been able to adapt their lives to their own limitations. They have contented themselves with living on a low physical and economic level. When, however, they are called to the army, it becomes necessary for them to adapt themselves to a new life—a life that is full of physical and nervous strain. It is then that they fail to come up to requirements, and that they appear in the light of pathologic subjects. In spite of the fact that our attention has been only directly called to the problem during the mobilization of the army, it is quite evident that the same problem exists in civil life and that it should be recognized and treated.

The various types of "effort syndrome" present a variety of clinical pictures. Underlying these long-standing or constitutional cases there are both physical and nervous elements. The importance of the physical element was brought out at General Hospital No. 9, at which it was shown that the muscular strength of many of these men is well below the average. Indeed, special tests showed that in a considerable proportion the general muscular condition was extremely poor. They had never taken much exercise, and had never been in good training. They were very "soft." One could hardly expect that they could stand up under any severe physical strain, for they had led for many years a sedentary life, and had devoted much energy to the avoidance of all physical exercise. It would, of course, take a long time to develop them to a point where they could march with full equipment. But the physical element is not the only factor of importance; there is also a large nervous element. Most of these men are very neurotic. They worry, are anxious,

and are easily upset. The man who has been presented to you told us that one of the things that bothered him most in his drilling was his anxiety lest the sergeant should find fault with him. They almost always have a great fear of "overdoing." They know from experience that when they overdo they "feel badly," and they fear that something serious may be about to happen to them. Unfortunately, the physician is not infrequently an important element of the production of this phobia. In a very large proportion of cases a doctor has said that they had a "weak heart," and has told them to do as little as possible. An anxious family has become worried about them, and has, in turn, done everything possible to limit their activities and to protect them from every kind of activity. Their lives center about their hearts. They are continually cutting down their activities. Instead of developing themselves physically, they have done exactly the opposite. Were the advice given by the doctor based on a proper comprehension of the case, the treatment might well be justified, but too often the diagnosis of "weak heart" shows that the clinical condition has been totally misunderstood. If there is disease of the heart, it is, except in very unusual cases, essentially disease either of the valves or the muscle, and in young persons the former is much the more common. It is probable that the diagnosis of valvular heart disease has frequently been made in the past when it did not exist, but as a result of our experience in examining large numbers of healthy men in the army, the profession as a whole has learned much about the presence of "accidental systolic murmurs," and doubtful presystolic rolls in normal hearts. Errors in the diagnosis of valvular disease should be much less common in the future. Myocardial disease, unaccompanied by valvular disease, on the other hand, is rarely met with in young people except as a result of syphilis, in association with hyperthyroidism or perhaps immediately after severe acute infections. In conditions other than these, in young persons, the diagnosis of "myocarditis" is open to doubt. In the type of case which we have under discussion it seemed of prime importance to determine whether there might not be some true myocardial involve-

ment, but investigations made in this country and in England have failed to show any definite evidence that this is the case. As far as the heart goes, the most that can be said is that there is an upset of the balance of the cardiac nerves. Whether this is principally due to an increased activity of the sympathetic system or a decrease of the vagus control is not at present certain. The exact mechanism by which the heart is affected so that it responds to slight exertion, or to nervous excitement by an abnormal increase in rate, is not at all clear, but the essential thing for us as practitioners is that we should recognize more frequently the so-called "irritable heart" in civil life, and should appreciate the fact that the cardiac element is purely secondary. The fundamental feature is probably a neurosis, and associated with this there is often a lack of general physical development. To lay stress on the heart in these cases is to create a semi-invalid. Experience has shown that it is much easier to direct a person's attention toward his heart than it is subsequently to draw his attention away from his heart, and the mobilization of our army has demonstrated how large a group of persons there are who are going through life, losing much of its joy and usefulness because of a heart disease that does not exist. The seriousness of an error of diagnosis in this type of patient can hardly be overestimated, for the neurotic, introspective temperament causes exaggerated anxiety, and the fear of injuring himself further results in the leading of a miserable existence. First, then, there must be a correct diagnosis. This will then lead to proper therapeutic measures. The physical aspect of the case will be treated by gradually increasing physical exercise and directions as to the leading of a normal healthy life. The nervous element is more difficult to handle. Encouragement, the instillation of self-reliance and self-respect, the direction of the attention away from bodily ailments and general psychotherapeutic methods are the essentials. But back of it all there lies too often the inherited neuropathic constitution, and one is reminded of the old saying that the most important thing for a child is the wise choice of his parents.

CLINIC OF DR. GEORGE CHEEVER SHATTUCK

MASSACHUSETTS GENERAL HOSPITAL

CASES FROM THE MALE MEDICAL CLINIC OF THE OUT-PATIENT DEPARTMENT

Case I.—Chronic Pulmonary Tuberculosis and Arteriosclerosis.

Case II.—War Nephritis and Chronic Adhesive Mediastinopericarditis Probable.

Case III.—Syphilis, Lesion of Aortic Arch, Probably Syphilitic; Healed Ulcer of Stomach or Duodenum.

April 9, 1919.

CASE I.—CHRONIC PULMONARY TUBERCULOSIS AND ARTERIOSCLEROSIS

No. 383,010—Frank W. Born in Connecticut, living in Boston. Age sixty-five, white. Occupation, bootmaker for twenty-five years, janitor for six years.

Present Illness.—The patient says that he has had coughs and colds every winter since a boy, that he coughs less in summer, raises about a tablespoonful of sputum, which is often thick and yellowish, but variable in appearance, and that he has never spit up blood. He has had no pain in the chest except occasionally with "indigestion not influenced by exertion."[1]

There has been gradual loss of weight for ten or twelve years aggregating about 40 pounds. For the same period there has been moderate dyspnea on exertion.

Past History.—Unimportant except as above stated.

[1] When a patient over forty years of age complains of "indigestion" be sure to exclude angina pectoris by determining whether the pain is brought on by exertion.

Family History.—Father died of "old age." Mother had *severe cough during the later years of her life.* A brother died suddenly with pain in the chest and shortness of breath. A sister died of "heart trouble." No tuberculosis or malignant disease known in the family.

Physical Examination.—Well developed and fairly well nourished. Brownish pigmentation across forehead irregular in outline. Pupils equal and react to light and accommodation. Knee-jerks present. Nasopharyngeal catarrh. Hoarseness.

Heart dulness not increased. No murmurs. Chest symmetrical, no shrinkage at apices. Lungs hyperresonant in front, slight dulness above right clavicle, breath sounds not definitely abnormal. Coarse râles at right apex in front, at both apices behind, and at left base. Abdomen negative.

Temperature 98.8° F., pulse 74, blood-pressure, systolic 190, diastolic 100. Urine, color normal, clear, acid; specific gravity 1018; no albumin or sugar.

DR. SHATTUCK: What is your diagnosis?

STUDENT: Chronic bronchitis.

DR. SHATTUCK: The physical examination does not warrant you in stating more, but that diagnosis should not be accepted as final. What are the three conditions which often pass under the name of chronic bronchitis?

STUDENT: Tuberculosis.

DR. SHATTUCK: That is the most important and commonest one. Can you mention another?

STUDENT: Chronic cardiac insufficiency.

DR. SHATTUCK: How does that resemble bronchitis?

STUDENT: There is chronic passive congestion and sogginess of the lungs.

DR. SHATTUCK: In such cases where are the râles most numerous?

STUDENT: At the bases of the lungs.

DR. SHATTUCK: Do you think that cardiac insufficiency is a factor in this case?

STUDENT: No. The râles are most numerous in the upper parts of the lungs.

DR. SHATTUCK: What is the third condition, often called "chronic bronchitis"?

STUDENT: Syphilis.

DR. SHATTUCK: That also should not be forgotten in cases in which the diagnosis is obscure, but it is not the disease I had in mind. I was thinking of bronchiectasis. Bronchiectasis is characterized by daily expectoration of purulent sputum varying in different cases from a teaspoonful to a cupful, generally more abundant in winter than in summer. It is a sequel of influenza and perhaps of bronchopneumonia independent of influenza. It runs an extremely chronic course, shows no marked tendency to shorten life, and interferes little with nutrition. In this respect it differs markedly from tuberculosis, in which, as you know, loss of weight is generally but not always a feature. In this connection I recall an autopsy on an old man who had extensive cardiac disease and tuberculosis for years. His death was due to lobar pneumonia, but active tuberculosis of unexpected extent was found. There was much fibrous walling off and caseation, showing the chronicity and slow extension of the process. During life, aside from dyspnea on the least exertion, the man was the picture of health. His skin was clear, color good, and nutrition excellent. Bronchiectasis differs again from tuberculosis in being generally confined to the bases. It may be unilateral or bilateral, may honeycomb and destroy large areas of lung tissue, or may be limited to a few small foci, showing on physical examination only a few râles. It is these slight cases which are generally called chronic bronchitis, but the more extensive ones often drift to sanatoria for tuberculosis in spite of repeated negative sputum examinations. In tuberculosis with abundant sputa tubercle bacilli should be demonstrable. It is the early case in which their absence need not excite surprise. Another feature of bronchiectasis which is important is the comparative absence of constitutional disturbance manifested by tachycordia, fever, and loss of weight, all which are generally present in tuberculosis. Its other manifestations are not related to the case under discussion. In our case the signs are in the

upper part of the lungs and not at the bases. This is strong evidence against bronchiectasis.

In favor of tuberculosis we have evidence of chronic pulmonary disease most marked at the apices and associated with constitutional disturbance, namely, marked loss of weight. The dulness at the right apex seems more than physiologic, but the absence of external shrinkage is noteworthy. Extensive dulness may be masked by the hyperresonance of emphysema. The normal pulse and temperature are not significant in a man of sixty-five, a time of life in which tuberculosis generally runs a slow course with little fever. Moreover, these are single observations made in the morning.

In summing up it may be said that tuberculosis should be suspected in every case of so-called chronic bronchitis, that in elderly persons it often presents atypical signs marked by emphysema, that the symptoms may be so slight and the onset so gradual as to escape the serious attention of the patient for many years.

The evidence in this case points first to tuberculosis. If this diagnosis cannot be confirmed, we will go over the ground again.

In addition, the patient has peripheral arteriosclerosis and probably renal arteriosclerosis. The high blood-pressure suggests the latter, and absence of albumin at a single examination does not exclude it. Although cardiac dulness is not increased, the heart is almost certainly hypertrophied. Palpation of the apex impulse in the left lateral position would probably show this. What further evidence is needed to establish a diagnisos?

STUDENT: Examination of the sputum.

DR. SHATTUCK: Yes, we will have an *x*-ray plate, too, to see what that will show, and I should like to have the larynx examined.

Second Visit (April 12th—three days after first visit).—Many medium moist râles at apices, more on the right than on the left. Few râles lower down. Bases clear. Sputum examination: Tubercle bacilli found.

x-Ray Report (by Dr. Holmes).—"Mottled dulness at both

apices to second rib in front on the right. General thickening and mottling of lung markings throughout the chest. Diaphragm excursion limited on both sides. Aortic arch tortuous and prominent." Interpretation: "Old tuberculosis at both apices, arteriosclerotic dilatation of aortic arch."

Throat Examination (by Dr. Barnes).—"No enlargement of arytenoids. Vocal cords roughened."

Final Diagnosis.—Advanced phthisis, arteriosclerosis.

Disposal.—Referred to Social Service for advice about hygiene and to arrange for sanatorium treatment to protect public.

April 21, 1919.

CASE II.—WAR NEPHRITIS AND CHRONIC ADHESIVE MEDIASTINOPERICARDITIS PROBABLE

No. 383,784—Jean L. Born in Canada, has lived most of his life in the United States. Age nineteen. White. Discharged soldier in Canadian Infantry.

Present Illness.—Captured by Germans on September 6, 1918, and sent at once to working camp, where he helped to build dug-outs. In the camp he was cold and wet most of the time. About September 15th he noticed swelling of the face, soon followed by edema of the ankles, which increased gradually. On September 23d he was relieved of work, but the swelling continued to increase. About the end of September he was sent to a hospital, where he spent two or three weeks. He was then transferred to another hospital in Antwerp, where he stayed ten days. From there he was sent to a prison camp, where there was a hut with stoves in it for the sick. While there his "stomach swelled way out." There was no dyspnea even at first.

On December 12th he was sent to a Canadian General Hospital at Boulogne, where for the first time he received systematic treatment and began to improve. His abdomen was tapped three times. On the 16th of December 3600 c.c. of clear watery fluid were withdrawn and on the 18th 7800 c.c., according to

notes forwarded with the patient. The notes continue as follows:

Dec. 16, '18: "Bl. p. syst., 188; diast., 124."
Jan. 1, '19: "Looking ill, marked dropsy, double detached retina."
Feb. 20th: "Feeling all right. Slight edema of shins and ankles. Was blind for three weeks. Now says there is a haze over eyes and can see only in brightest light. Pulse good and slow. Fluid still present in abdomen. Patient looks white and anemic."
"Urine: albumin + +, pus and hyaline casts."
March 6th: "Alb. retinitis, vision less than 6/60."
"Urine: pus, hyaline and granular casts about 40–50 ounces.
"The patient says that sight is steadily improving, that he sees well now, that his appetite is excellent and that he feels better in every way."

Past History.—Diphtheria and measles when a small child, tonsillectomy at age of ten; no scarlet fever or rheumatic fever.

Physical Examination (April 21, 1919).—Well developed and fairly well nourished. Skin and mucous membranes of good color. Pupils equal and react to light and accommodation. Albuminuric retinitis, slight. Throat negative. Several carious teeth. Tongue coated.

Heart.—Apex impulse visible and palpable in fourth space within nipple line. Dulness slightly increased to right and left. Action regular and not rapid. Aortic second sound much accentuated and ringing. After slight exertion a faint systolic murmur is heard at the apex. In the left lateral position the apex impulse is felt a little beyond the anterior axillary line. The force and width of the impulse are increased. Blood-pressure: Syst., 185; diast., 135.

Lungs and *abdomen* negative. Knee-jerks exaggerated. The skin of the abdomen, thighs, and knees shows numerous and well-marked lineæ albicantes. No edema.

Urine: Cloudy, specific gravity 1019, albumen + +, many leukocytes and granular casts.

Temperature 99° F. Pulse 72. Weight 144 pounds.

Second Examination (April 23d).—Slight systolic retraction of chest wall below nipple and over tenth and eleventh ribs in

posterior axillary line. Pulsus paradoxus slight in degree. In recumbent position soft systolic murmurs are heard in the pulmonic area and in the mitral area, not transmitted to the axilla. There is also a short diastolic murmur heard near the mitral area.

Aortic second sound loud and ringing as before. Pulmonic second sound also accentuated. Blood-pressure: Syst., 165; diast., 110.

DR. SHATTUCK: What is the diagnosis?

STUDENT: Nephritis.

DR. SHATTUCK: Why is the apex in the fourth interspace?

STUDENT: Perhaps the heart was pushed up by the ascites and became adherent.

DR. SHATTUCK: Does the heart move with change of position?

STUDENT: Yes. The apex impulse moves to the left when the patient lies on the side.

DR. SHATTUCK: The cardiac dulness on the right shifts also, so that the conclusion seems justified that adhesions if present are not very extensive, but there might, I think, be some adhesions nevertheless. In favor of their existence is the retraction of the chest wall and ribs near the apex of the heart, and in the back.[1] The pulsus paradoxus points the same way, but is of little diagnostic value. The pronounced ascites is very unusual in a renal case in which the heart has not been overtaxed. In this case there is no reason to believe that the heart was a factor in the dropsy. I do not remember having ever seen paracentesis done for ascites in uncomplicated nephritis, but in this case large amounts of fluid were thus removed, and tapping was required three times. The prominence of the ascites in the clinical picture suggests chronic adhesive mediastinopericarditis as a possible cause, and the signs of adhesions above referred to strengthen this hypothesis.

The force and width of the apex impulse as felt in the left lateral position point to hypertrophy, probably moderate in

[1] A very much hypertrophied heart without adhesions may cause retraction near its apex, but in this case hypertrophy is slight.

degree. If there were dilatation of more than a slight degree the apex would be farther out or farther down. The increase of blood-pressure three times recorded is consistent with hypertrophy. The murmurs next require explanation. The answer is not clear to me. The systolic murmurs in the pulmonic and mitral areas may be the same and may be functional or due to slight relative insufficiency of the mitral valve. Perhaps the systolic murmur at the base is produced at the aortic valve, but if so it is heard in an unusual position. It seems probable that the diastolic murmur is of aortic origin, for it is not of the presystolic type nor is there any accentuation of the first sound to suggest mitral stenosis.

On the whole, it seems probable that there is a well-compensated lesion of the aortic valve of slight degree and perhaps of the mitral as well. The lesion may have developed in childhood as a result of infection from the tonsils which were removed, or it may be associated with the nephritis, as heart lesions often are in the glomerulonephritis of civil life. I do not remember to have seen a heart lesion develop in a case of war nephritis.

The diagnosis, in brief, is:

1. Subacute glomerulonephritis beginning under war conditions.

2. Hypertrophy of the heart with little or no dilatation.

3. Chronic endocarditis of the aortic valve, slight in degree, seems probable.

4. Albuminuric retinits.

5. Chronic adhesive mediastinopericarditis seems probable.

War nephritis is an acute nephritis. In civil life acute nephritis is mainly a disease of childhood, but acute exacerbations of chronic glomerulonephritis in the adult are common and may simulate acute nephritis. In war nephritis the kidney lesions are very like those of acute glomerulonephritis. Acute glomerulonephritis has been shown to be of bacterial origin, so that by analogy war nephritis should be of similar origin, but proof is lacking. Having seen war nephritis common in the spring, scarce in the summer, and recurring in greater numbers again

in the autumn of three successive years in France, I am convinced that exposure to cold and wet is a factor in the great majority of cases. I believe also that infection plays the decisive part.

The absence of dyspnea at the outset in this case is strikingly unusual, for the patient was doing heavy work. A common story is that the patient became short of breath while marching with equipment, that the dyspnea increased from day to day until he was obliged to fall out, and that later edema of the ankles or face was noticed.

The *prognosis* is uncertain. The mortality in the acute stage of war nephritis is very low. Uremic symptoms when they occur generally yield readily to treatment. Undoubtedly a certain proportion of cases become chronic and will die ultimately of the disease, but what this proportion is cannot yet be known. The rapid improvement of most cases offers hope of cure in a large proportion. In this case the pus in the urine and the duration of the illness seem to me unfavorable signs, and I think the case is passing into the chronic stage.

Treatment requires limitation of foods, the waste of which is mainly eliminated by the kidney. Water need not be restricted in this case, for the heart is strong and the absence of edema shows ability of the kidney to excrete water.

Salt need not be forbidden entirely, although it might be unwise for the patient to take much of it. We may tell the patient to use salt sparingly, but a strictly salt-free diet is quite unnecessary.

The patient is gaining in weight and strength and shows little sign of anemia now. It would be a mistake to put him on a much restricted or monotonous diet, of which he would soon grow tired, because he would be unable to eat enough to maintain himself in good general condition. Now that the acute stage has passed and the appetite has returned, the patient may eat a little meat or fish once daily and eggs need not be restricted. Starchy foods and vegetables of any kind can be eaten freely. Acids, highly spiced foods, meat broths, and alcohol should be avoided.

Drugs are not needed at present. Exposure to cold must be avoided. Woolen underclothing should be worn. Physical exertion should be moderate. If appetite fails or if headache or edema should be noticed, the patient should at once restrict the diet and return to the hospital. In any case, he is to report once a month.

March 31, 1919.

CASE III.—SYPHILIS, LESION OF AORTIC ARCH, PROBABLY SYPHILITIC; HEALED ULCER OF STOMACH OR DUODENUM

No. 382,260—William P. Age fifty-nine. White. Married thirty-seven years. Occupation, teamster for forty years.

Family History.—Wife and 5 children living and well. One child died of pneumonia and another shortly after birth, cause unknown. There were no miscarriages.

Past History.—Says he has had indigestion for ten or fifteen years, with epigastric pain from one to two hours after meals, and sometimes keeping him awake until midnight. No sharp attacks like biliary colic. Vomiting has been frequently associated with the pain. Vomitus sometimes watery and sometimes containing much food. Ten years ago he vomited a pint of blood, but this has not recurred. Stomach trouble now is slight.

Thinks he had syphilis twenty years ago and had received little treatment for it. Nocturia two or three times for years.

Present Illness.—Dyspnea on exertion for six months, but never associated with pain, he thinks. Has been doing heavy lifting, but aside from moderate dyspnea, which soon passes off, has observed no ill effect.

Physical Examination.—Well developed, obese. Pupils small, equal, and react normally. Teeth poor. Throat negative.

Heart.—No clearly demonstrable enlargement. Action not rapid, but when first examined there was an irregularity recurring with every fourth beat. Half an hour later only an occasional premature systole was heard. No murmurs were heard. Blood-pressure: systolic 150, diastolic 120.

Lungs negative. *Abdomen* negative.

Knee-jerks sluggish. Varicose veins on both legs and moderate edema to knees. Temperature 98.6° F. Weight 235 pounds.

DR. SHATTUCK: What do you think is the matter with this patient?

STUDENT: Duodenal ulcer.

DR. SHATTUCK: Why has he edema of the legs?

STUDENT: That is probably due to the varicose veins.

DR. SHATTUCK: The past history is strongly suggestive of gastric or duodenal ulcer. The type of pain, the duration of symptoms, and the vomiting of blood all point to this conclusion, but the symptom which seems to me of chief importance now is the dyspnea. Although the heart shows little evidence of enlargement, the chest wall is so thick as to render percussion valueless. I should not be willing to say that the heart is normal without further evidence. The premature systoles in a man of fifty-nine years of age are more significant than they would be in a young man, and in this case they may indicate myocardial changes of an important kind. Moreover, the edema of the legs may not all be due to the veins. Before making a final diagnosis we must have more evidence, but I believe that the heart is beginning to weaken and that the patient should be treated accordingly. The recognition of slight signs of failing compensation is very important, for in such cases much good may often be accomplished.

There is another question which merits consideration at this time. If it be assumed that the myocardium is weak, what is the etiology? Physically the patient is not senile nor does he show the marked degree of peripheral arteriosclerosis so common in senility. The past history gives one important clue, namely, that the patient thinks he had syphilis twenty-one years ago. The family history is non-committal, but evidence of active syphilis should be looked for in this case nevertheless.

We shall want *x*-rays of the heart and aorta and of the gastro-intestinal tract and a Wassermann test.

Treatment.—Epsom salts, 2 tablespoonfuls[1] every other day before breakfast, and tincture of digitalis, min. x t. i. d.

April 1st: Wassermann test strongly positive. *x*-Ray report by Dr. Holmes: "Well-marked evidence of hypertrophy of left ventricle. Shadow of great vessels increased. Gastro-intestinal tract negative."

April 3d: Second visit. Iodid and mercury prescribed.

April 15th: Third visit. Feels much better. Dyspnea less. indigestion slight. Pulse not rapid. Occasional premature systole. Blood-pressure 145 systolic and 100 diastolic. After climbing two flights of stairs pulse 108.

Heart: Sounds distinct, none accentuated. No murmurs heard in the sitting position. When the patient lay on his back a faint systolic murmur was heard in the aortic area when the lungs were deflated and the breath held. In the left lateral position the apex impulse was felt in the anterior axillary line and a soft systolic murmur was heard at the apex.

Referred to South Medical Department for treatment of syphilis. They administered 0.1 gm. diarsenol intravenously.

Further Discussion of Case.—When a heart is much enlarged the apex impulse, as a general rule, can be felt in the fifth or sixth space in the *midaxillary* line when the patient lies on his left side.

In this case the impulse moved only to the *anterior* axillary line and it was not noticeably increased in force. I think, therefore, that the enlargement of the heart suspected at the first examination and reported by the radiologist is slight in degree. The heart is not notably dilated.

The murmur at the aortic area indicates a slight lesion of the valve or of the arch. The arch has been shown to be slightly enlarged, but the enlargement is not of the type characteristic of syphilis in that it is not limited to the first part of the aorta. If it were so limited, syphilis of the arch at an early stage would be extremely probable from that evidence alone.

[1] The large dose of salts will help to reduce weight, which is essential in obesity associated with cardiac weakness.

The murmur was probably overlooked at the first examination. These incipient murmurs are generally overlooked unless sought for with the greatest care. When syphilis involving the heart or aorta is suspected, systolic and diastolic murmurs should be looked for most carefully. Deflation of the lungs and examination in the left lateral position will reveal many murmurs that would not otherwise be found. When found, they increase the probability of syphilis as a factor, unless they can better be explained on some other hypothesis. They are less important in senility, because at this period of life they are commonly the result of degenerative changes. When such a murmur is found before the patient has reached the age of thirty it is generally attributable to an endocarditis of bacterial origin. The possibility of syphilis as a factor in the case should not be forgotten either in the young adult or in the aged, but when a heart lesion is first discovered between the ages of thirty-five and fifty the probability, *a priori*, is in favor of syphilis as the cause. This fact cannot be too strongly emphasized because early diagnosis gives hope of good results from treatment, but after the damage has become extensive no treatment can cure, and the prognosis in such cases is grave even with the best treatment.

Another interesting possibility exists in this case. Might the stomach trouble also have been due to syphilis? Cases of ulcer with hematemesis have been attributed to syphilis more and more frequently in recent years. Whatever the cause in this case, the lesion seems to have got well without leaving any signs discoverable by *x*-ray examination.

April 24th: Fourth visit. Patient feels about the same. Slight dyspnea persists. Less edema of legs. Left leg swells occasionally. Pulse-rate at rest 84. After climbing two flights of stairs quickly it reached 124 and showed occasional irregularity. Diarsenol 0.1 gm. administered by South Medical Department.

Final Diagnosis.—Syphilis, lesion of aortic arch, probably syphilitic. Healed ulcer of stomach or duodenum, perhaps syphilitic.

Disposal.—Undergoing treatment.

CONTRIBUTION BY DR. ARIAL W. GEORGE
AND DR. RALPH D. LEONARD

THE USE OF THE *x*-RAY IN THE STUDY OF MULTIPLE DIVERTICULITIS OF THE COLON

Recognition of Diverticulitis as a Clinical Entity; Constipation as an Etiologic Factor; Pathologic Changes; Symptoms; Differential Diagnosis; Radiographic Classification of Multiple Diverticula; Bibliography.

THE term "multiple diverticulitis," when applied to the large intestine, refers to the presence of one or more sacculations projecting from the exterior of the gut, together with their secondary inflammatory changes. As many of these pathologic sequelæ involve the tissues around the intestine, "peridiverticulitis" might be a more apt term.

Diverticulitis today occupies an important place in medical literature and is recognized as a distant clinical entity by every operating surgeon of large practice. It is only within the past twelve or fifteen years that the profession has had an intelligent appreciation of the importance of this condition, although Graser presented in 1898 a fairly accurate clinical and pathologic description of "diverticulum formation" in the large bowel and showed that such cases were not uncommon.

Previous to Graser's work, however, the literature on "diverticulitis" consisted in the occasional report of isolated cases. Virchow in 1853 described certain "pathologic changes involving the descending colon and sigmoid characterized by isolated, circumscribed, adhesive peritonitis." He even described some of the possible complications, adhesions, constrictions, perforation, etc. He did not, however, note the presence of diverticuli

as the original cause, considering constipation as the etiologic factor, neither did he attempt to describe the clinical picture.

From 1900 on many important contributions were offered, particularly by American observers. Fisher in 1901 and Beer in 1904 did experimental work on the etiology of the intestinal diverticula. In 1907 the Mayos, Wilson, and Griffin reported several operated cases of diverticulitis, contributing particularly to the clinical aspects of the disease. In the same year Brewer offered a paper also describing the clinical manifestations of diverticulitis entitled "Etiology of Certain Cases of Left-sided Intra-abdominal Suppuration." In the following year Ashhurst reported a case of "Sigmoid Diverticulitis" in a child. This patient is the youngest case on record. McWilliams about the same time reported cases emphasizing some of the serious sequelæ.

Telling in 1908 for the first time collected and analyzed the recorded cases, classifying the pathologic changes and clinical results. This classification has furnished the basis for most articles of importance written since that date. In 1911 Telling and Gruner amplified this classification, basing their conclusions on a much larger number of cases.

During the last seven or eight years there have been many contributors to both the clinical and pathologic features of "multiple diverticulitis," among whom are Mayo, Wilson, Giffin, Hartwell and Cecil, Graves, Erdmann, and particularly McGrath. His paper on the "Etiology and Pathogenesis of Colon Diverticula" is particularly valuable.

The *x*-ray as a means of diagnosis of multiple diverticulitis was first brought to our attention by Dr. Stewart, who made a Roentgen diagnosis of sigmoid diverticulitis in a case reported by Abbe in August, 1914.

Carman, in November of the same year, and Case, in the following year, described the radiographic appearance of multiple diverticulitis of the colon. Since then a few contributions on this subject have been made by roentgenologists to periodicals and text-books. These papers, however, are in the nature of

reviews and confirmation of Carman and Case's work, and offer nothing particularly new.

In order to better understand the radiographic appearance of multiple diverticulitis it may be wise to consider some of the pathologic aspects. The following statements and classifications represent in general a résumé of the more recent contributions to the pathology and etiology of this disease.

Diverticula may be classified in two general groups—the congenital group and the acquired group. The congenital group is small. Meckel's diverticulum in the small intestine and a few other developmental anomalies, such as a persistent urachus, compose this class. These congenital diverticula do not enter into the scope of the present paper.

As Dr. Charles Mayo states, "The various hollow viscera and tubular structures of the body are subject to acquired diverticula. Even the large blood-vessels are prone to this condition in the form of sacculated aneurysm."

The group of "acquired diverticula" comprise practically all the diverticula which are of clinical importance. The esophageal diverticula, the various diverticula of the duodenum, ileum, and the multiple diverticula of the large intestine, in which we are particularly interested, belong to this group.

The acquired diverticula are further described as "true" or "false," these terms being used with reference to the structure of the walls of the diverticulum, as compared to the structure of the walls of the normal organ. Some pathologists use the terms "complete" and "incomplete" synonymously with "true" and "false."

A "complete" diverticulum presents in its walls the same tissues and same arrangement of lining membranes as the normal intestinal wall. The "incomplete" or "false" diverticula consist of but part of the elements found in the normal intestinal wall. The diverticula of the colon probably belong to this latter group, their walls being composed of merely the mucous and serous coats. There is no "muscularis" as found in the normal intestinal wall. McGrath speaks of these diverticula as "hernia mucosæ."

It has been suggested that originally they were "true" diverticula, the muscle coat simply atrophying from disuse. In view of the probable etiology of diverticula we feel that the idea of "muscle atrophy" is rather unlikely.

Diverticula of the large bowel may be found in any division of the large intestine, but are most commonly found in the descending colon and sigmoid. McGrath's figures in a series of 32 cases are typical. In 27 cases diverticula were found in the descending colon and sigmoid, 2 cases in the rectum, 1 case in the transverse and hepatic flexure, and 1 in the anal ring.

Our observations as radiologists would lead us to believe that diverticula occur in the ascending and transverse colons more frequently than has generally been believed. The diverticula in this location, however, are less likely to give symptoms than in the descending colon and sigmoid, hence do not come to the attention of the surgeon or pathologist.

The number of diverticula present may vary from 1 to 100 or more. Hauseman found 400 at autopsy in a man of eighty-five dying from pneumonia. It is generally agreed that colon diverticula are multiple and that 10 to 20 are the average number found.

They vary in size from a small fraction to 2 or more inches in diameter. The tendency is to gradually increase in size, the earliest stages being microscopic. The average size found at autopsy or operation is about that of a pea.

They are of variable shape, being usually round or ovoid. Some are distinctly pedunculated, with a minute opening into the lumen of the intestine.

The contents of these pockets is almost entirely fecal material, the consistency of which is variable. Occasionally the fecal material becomes so inspissated as to produce fecaliths. McGrath speaks of "concretions becoming incapsulated within the diverticula and, the pedicles sloughing, give rise to free bodies in the abdominal cavity." Numerous writers have reported foreign bodies in the diverticula.

The diverticula project from the exterior of the gut, usually close to the mesenteric attachment (Figs. 254 and 255). They

may be found between the two layers of peritoneum forming the mesentery. It is also observed that the diverticula are in close proximity to the epiploic appendices.

Under the microscope the walls of the diverticula are seen to consist of mucosa, usually submucosa and serosa. There is

Fig. 254.—Diverticula of sigmoid. The pouches are, for the most part, into the appendices epiploicæ. (Taken from Maxwell Telling and Gruner, British Journal of Surg., vol. iv, No. 15.)

complete absence of smooth muscle-fiber. In some of the larger diverticula the lining of epithelium is more or less obliterated, due to the continued pressure of the fecal contents.

There is no obvious reason for believing that the formation of a simple colon diverticulum will necessarily be the source of

symptoms. In fact, we frequently find evidence of diverticula on the *x*-ray plate without the patient presenting any local symptom. It is apparent that only when pathologic changes take place that are secondary to the diverticula do the patients

Fig. 255.—Portion of descending colon. Specimen laid open to show the internal orifices of the diverticula. (Taken from Maxwell Telling and Gruner, "British Journal of Surg.," vol. iv, No. 15.)

complain. It is difficult to estimate what percentage of diverticula have inflammatory changes such as to produce symptoms. Telling estimates that 60 per cent. of all persons having colon diverticula may have symptoms.

It is clear, therefore, that the recognition of inflammatory sequelæ is of utmost importance in the consideration of multiple diverticulitis. In general, the various secondary changes and complications are the result of infection through the walls of the diverticula. They have been classified for convenience in various ways. The following is as typical as any:

(*a*) *General peritonitis* may be produced by the actual passage into the peritoneal cavity of bacteria or their toxins through the thinned-out walls of the diverticula, some of the walls being so thin as to consist only of peritoneum.

(*b*) Acute gangrenous inflammation may result from strangulation at the neck of the pedunculated type of diverticulum.

(*c*) The chronic proliferative extramucosal inflammation is the most constant pathologic process. Telling considers this condition the most important. These proliferative changes produce in time large palpable masses. These masses tend to surround the gut. Embedded in them are the diverticula. Later they tend to actual intestinal obstruction. It is this type of inflammation to which the term "peridiverticulitis" applies, and it is this complication which is frequently diagnosed as cancer or sarcoma.

(*d*) It is evident that, with a mass of connective tissue in close proximity to other organs, adhesions involving these organs will arise. The bladder, small intestine, and pelvic organs are the viscera most commonly affected.

(*e*) *Perforation* is one of the most serious complications. This may be *acute*, perforation taking place through the thinned-out diverticulum wall or possibly through an ulcerated area. This type of perforation may follow severe strain. Chronic perforation may slowly take place into the peridiverticular mass of connective tissue. This may be associated with abscess formation. Fistulæ connecting the colon with the bladder or small intestine may follow a chronic perforation.

(*f*) Chronic inflammation of the mesentery as a complication of diverticulitis has been reported by several, among them Telling and McGrath. The late changes in mesenteritis are of importance, in that contracting bands of connective tissue in

the mesentery may be an etiologic factor in the production of some cases of volvulus.

(*g*) The development of *cancer* on the inflammatory mass is a possibility. The condition is analogous to the development of cancer on a chronic indurated gastric ulcer. McGrath reports that in his series of advanced peridiverticulitis with formation of a mass of connective tissue, 25.9 per cent. showed evidence of malignancy.

Beer, Wilson, Telling, Giffin, McGrath, Hartwell, and Cecil have all presented theories as to the cause of diverticula. The following factors are worth consideration:

1. Age: Most cases occur in people beyond middle life. Occasional cases are reported in patients under thirty. Ashhurst reports a possible case of seven years.

2. Males are twice as susceptible to diverticula as females.

3. Obesity seems to be a definite predisposing cause; on the other hand, rapid loss of weight may be followed by diverticulitis.

4. The normal muscle structure of the colon, particularly the arrangement of the muscle-fibers, is thought to predispose toward diverticulum formation.

5. The physiologic rôle of the sigmoid, in that it contains gas and fecal material under more or less pressure, may be an etiologic factor.

6. The points of entry for blood-vessels passing through the intestinal wall seem common sites for diverticula. These points of entry are also close to the appendices epiploicæ.

7. Another predisposing factor may be a variation in the size of the blood-vessels as found in congestion from venous obstruction, or high arterial pressure in cardiorenals or advanced arteriosclerosis.

8. There may be a congenital predisposition.

9. Simple muscle weakness in the intestinal wall may have a causal relation to the presence of diverticula.

One or all of the above factors may be involved in the production of diverticula. In general, herniæ of any kind are the result of *increased pressure* within a cavity plus a *local weakness* in the wall. In the region where diverticula most commonly

occur (the sigmoid) the intestine is subject to *increased pressure* from accumulating feces and gas.

Weakness in the wall may be produced by localized fatty degeneration of the muscle; degeneration from cachexia; the foramen for the blood-vessels with the coat of connective tissue are less resistant than the surrounding muscle-fiber, etc.

Multiple diverticulitis presents a fairly definite clinical picture. The average age of the patient is from forty-five to sixty and, in general, there is a marked tendency to obesity. In our cases diagnosed by the *x*-ray the majority of the patients weighed about 200 pounds. Men seemed more susceptible than women.

A history of chronic constipation is found in about one-quarter of the cases. A picture of chronic obstruction with alternating diarrhea and constipation is suggestive, the chronic obstruction being from the secondary connective-tissue changes.

Pain is present in a large percentage of cases. In the chronic type there is frequently a long history of attacks of crampy pain in the left lower quadrant. About 15 per cent. give a story of abdominal pain of considerable severity. It must be remembered that symptoms are the result of the secondary pathologic changes. These may vary all the way from acute peritonitis to acute obstruction, so that the symptoms of pain may be variously manifested.

The simple diverticula without secondary inflammation changes probably do not give symptoms.

A palpable tumor in the left side is found in about 30 per cent. of the cases giving symptoms. It is usually an elongated "sausage-shaped" mass lying commonly just above and more or less parallel with Poupart's ligament. Frequently it is mobile. A characteristic of this tumor is its variability. It may appear and disappear several times, its appearance being accompanied by signs of inflammation.

Abscess formation, local peritonitis, obstruction, etc., all show their usual clinical signs of fever, leukocytosis, pain, etc.

Rectal examination is negative in all cases except where there is actual diverticulum formation in the rectum itself. The proctoscope reveals nothing.

Multiple diverticulitis is mainly an extramucosal disease of the intestine, so that commonly the mucous membrane remains intact. As a result the passage of macroscopic blood is not commonly associated with diverticulitis. This is an important point in the differentiation of cancer. Carcinoma is a mucosal disease and associated with bleeding.

In the differential diagnosis carcinoma of the colon is the important condition to be ruled out. The pathologists tell us that possibly 25 per cent. of the chronic indurated diverticulitis cases become malignant.

But, in general, a patient who is well nourished and continues to maintain good nutrition in spite of symptoms; who has a long history of attacks of abdominal pain, localizing in the left lower quadrant; who presents at times a palpable mass in the left lower quadrant; usually who has not passed macroscopic blood; who may present evidence of vesical fistulæ; and with a negative sigmoidoscopic examination—such a patient may reasonably have made a diagnosis of chronic proliferative diverticulitis.

In carcinoma of the colon there is usually an early loss of flesh. Pain is not a constant symptom until obstruction sets in. Tenderness is a late finding. Blood, on the other hand, may be an early finding. When tumor is present, it is permanent.

From the other forms of pelvic inflammation it may be difficult to differentiate multiple diverticulitis. Left-sided appendix can usually be ruled out by the *x*-ray. In the presence of a palpable left-sided tumor one must always consider diverticulitis.

Up to the present time roentgenologists have perfected no special technic for visualizing colon diverticula. Such cases of multiple diverticulitis as have come to our attention have been found in the course of routine *x*-ray intestinal examination.

For those roentgenologists who do not make a routine practice of radiographing the abdomen previous to the adminstration of the barium meal we wish to emphasize the importance of this preliminary study. Just as preliminary routine plates of

the right upper quadrant will occasionally visualize a gall-stone, so plates of the left lower quadrant oftentimes will give evidence of importance in the question of multiple diverticulitis.

From the pathology we learn that fecaliths may be found in the diverticula due to the prolonged retention of fecal material. On account of the deposition of calcium the fecaliths are capable of casting distinct shadows on the *x*-ray plate. Unless preliminary plates are made, such shadows will be obscured by the barium meal.

Diverticula, which have become separated from the intestine, and are free bodies in the abdominal cavity, may produce a shadow on the plate. Their free movement will be demonstrated.

These preliminary plates may also reveal shadows, which later in the examination might lead to confusion, unless their presence had been previously recognized. Calculi in the left kidney or ureter; calcified glands, retroperitoneal or mesenteric; phleboliths; sclerosis of iliac arteries—all may produce shadows somewhat simulating the contents of diverticula.

The plates should be made both on the front and back. In our experience an intensifying screen allows us to use a little less penetrating ray, resulting in a more contrasty plate. This additional contrast, slight as it may be, frequently makes all the difference between showing and missing an obscure shadow. The fluoroscope helps in differentiating a movable and fixed shadow, and particularly in determining if it moves with respiration.

After the preliminary examination the patient is given the opaque meal. The meal which has been used routinely for several years in general gastro-intestinal examinations has proved satisfactory for the demonstration of colon diverticula. It consists of 2 glasses of buttermilk with $1\frac{1}{2}$ ounces of barium sulphate in each glass. This is taken on an empty stomach.

With the buttermilk meal the appendix is more readily filled than with other meals, so it is likely that diverticula are more readily filled with this type of meal.

Twenty-four hours after the meal we find the best filling of the colon. It is on this plate that the diverticula are first

visualized. As a frequent site for the diverticula is near the mesenteric attachment, it is obvious that in a simple antero-posterior plate these shadows may be hidden by the mass of barium filling the lumen of the colon. Palpation under the fluoroscopic screen or stereoscopic plates may bring to light some of these hidden diverticula (Figs. 256–259).

As these pockets tend to retain the barium over a prolonged period, we have found that plates made thirty-six to forty-eight

Fig. 256.—Normal colon. Plate made following a barium enema.

hours after the meal show the diverticula to the best advantage. At this time the lumen of the colon will be entirely free of the barium meal, and the barium-filled diverticula stand out clear and distinct.

It is of importance to determine the length of time barium is retained in these pockets. This, of course, is variable and de-

pends upon the type of diverticulum. We have observed cases where plates made not only days but weeks after the meal still showed evidence of barium in the diverticulum.

The examination with the barium meal should always be followed up with the barium enema. The enema is not as satisfactory as the meal for visualizing the actual diverticula. The pockets do not fill readily, perhaps for the same reason that the

Fig. 257.—Normal colon. Plate made twenty-four hours after a barium meal.

appendix is not filled by the enema. Then again the colon is usually so distended by the enema that the mass of barium very easily obscures many of the diverticula. The enema is of value, however, in bringing out some of the secondary pathologic changes, such as chronic thickening of the intestinal wall, with narrowing or beginning obstruction; abscess cavities, chronic perforation, fistulæ, etc.

Our practice is to mix up 5 or 6 ounces of barium with a pint

of buttermilk and water enough to make a quart. This is given slowly with very little pressure; the elevation of the container usually not more than 2 feet above the table. A soft rubber rectal tube is used, the end being inserted just beyond the internal sphincter. The patient, if possible, lies on the left side.

This solution is not irritating, and the patient usually retains it comfortably for ten minutes or more. Plates and study with

Fig. 258.—Normal colon. Plate made after a barium meal. Some hypertonicity. Note appearance of haustra in transverse colon, likely to be confused with diverticula.

the fluoroscope are made immediately. In fact, it occasionally gives valuable information to watch the abdomen with the fluoroscope as the enema is being given.

The patient is next asked to empty the colon as completely as possible, and further plates are made. These last plates will visualize any diverticula which retain the barium, and also

give us information as to the ability of the patient to empty the colon.

The various radiographic appearances of multiple diverticula roughly group themselves into three general classes. This radiographic classification corresponds with the grouping based on their pathology.

The *first class* is composed of cases showing simple diverticu-

Fig. 259.—Normal colon. Following a barium enema. Note the atonic condition of the intestinal walls.

lum formation. The diverticula may be diffusely scattered throughout the colon. The patient may or may not have symptoms.

The *second group* consists of those cases showing beginning secondary inflammatory changes. These cases usually show the diverticula pretty well localized about the descending colon and sigmoid. The patients usually are having symptoms.

The *third group* consists of cases showing advanced secondary inflammatory changes, such as pericolitis, tumor, obstruction, etc. (Figs. 273–277).

Group 1.—Occasionally, in the course of the routine gastrointestinal examination, one will observe in the plate made twenty-four hours after the meal round discrete shadows of the

Fig. 260.—Multiple diverticula. Plate made twenty-four hours after meal. Diffuse distribution of the diverticula over transverse colon, descending colon, and sigmoid. Simple diverticulum formation without inflammatory changes. Class I.

same density as the barium-filled colon, but usually distinct from it. The shadows vary in size from that of a pinhead to a dime or larger. They are circular in outline and are in close proximity to the intestinal wall. Under the fluoroscopic screen they seem to be a part of or intimately connected with the wall, yet distinctly outside the lumen of the intestine.

These shadows represent the barium-filled diverticula. They may be seen anywhere throughout the entire colon from the cecum to the rectum. Any portion of the circumference of the gut may be affected. As these diverticula have a tendency to retain the barium, as mentioned before, the best time to observe them is thirty-six to forty-eight hours after the meal, at which

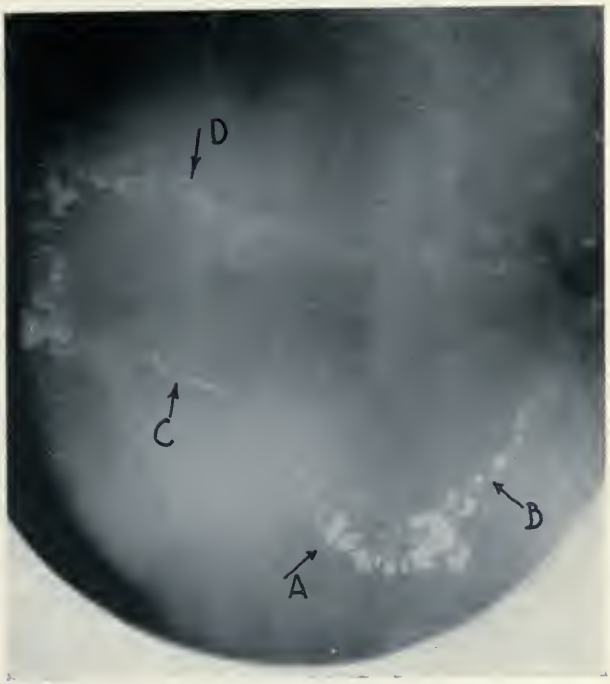

Fig. 261.—Multiple diverticula. Plate made twenty-four hours after barium meal. A few simple diverticula diffusely distributed at *A*, *B*, and *D*. Appendix visualized at *C*. Patient has no symptoms. Class I.

time the lumen of the intestine is free of the barium and the round discrete shadows of the barium in the diverticula stand out clearly.

These shadows, varying in number, may be seen anywhere along the course of the colon, the most likely site being the descending colon and sigmoid. In some of the extreme cases the diverticula appear very much like a string of beads.

The diverticula classified in this first group are frequently not associated with symptoms. They are occasionally found during a routine examination in people apparently well.

As the condition is one of a simple diverticulum formation without inflammatory changes, about the only symptoms to be expected would be those of toxic absorption, the absorption being from the prolonged stasis of fecal material in the diverticula.

Fig. 262.—Multiple diverticula. Plate made twenty-four hours after barium meal. No symptoms; no inflammatory changes. Class I.

Two conditions may present radiographic pictures likely to be confused with simple diverticula. *First*, a hypertonic condition of the colon may be associated with almost a spastic condition of the haustra, so that discrete masses of barium become separated from the mass of barium in the lumen. The dependent portions of the haustra of the transverse colon seem to be a common location. The plates made at intervals will demonstrate

Fig. 263.—Simple diverticulum. Plate taken after barium enema. Class I.

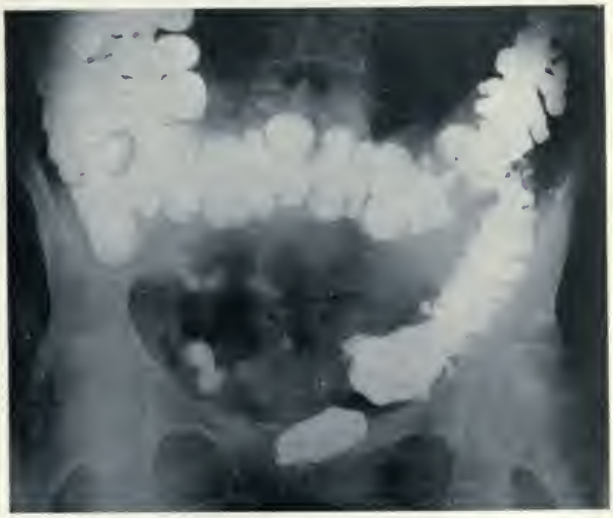

Fig. 264.—Multiple diverticula. Plate made after a barium enema. Two diverticula seen. Class I.

that these apparent sacculations are only temporary. A true diverticulum is permanent. Again, study with the fluoroscope and barium enema will show that these haustral shadows are within the lumen of the gut and are not extramural, as is the case with the diverticulum.

Second, in a certain type of individuals the colon contents become subdivided into small discrete masses, particularly in

Fig. 265.—Multiple diverticula after a barium enema. A few small diverticula. Class I.

the descending colon and sigmoid. A spastic type of constipation frequently produces this condition. These small masses may be confused with diverticula. In inconstancy of these shadows is the chief means of differentiation.

Group 2.—The second group in the classification of diverticulitis is composed of cases showing beginning secondary changes of an inflammatory nature. The diverticula in this

group are usually localized along the lower descending colon and sigmoid. The patients invariably have more or less definite symptoms.

The *x*-ray plate shows numerous diverticula ranging from 4 or 5 to 20, situated in a limited region about the junction of the sigmoid and descending colon (Figs. 266–272).

The amount of intestine involved is not more than 2 or 3 inches. The important radiographic appearance differen-

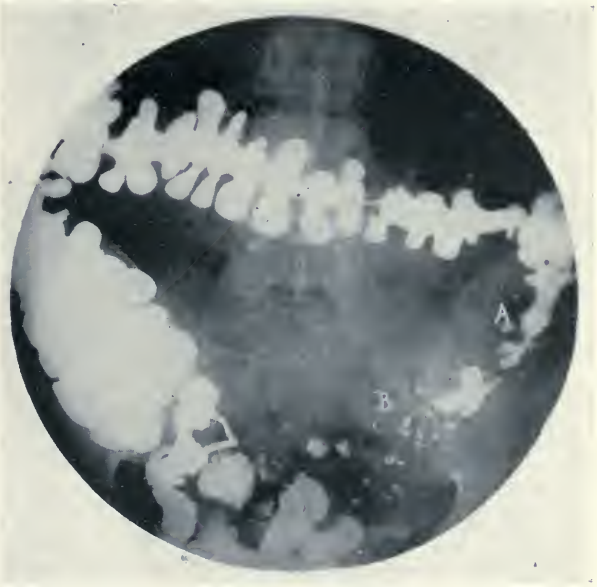

Fig. 266.—Multiple diverticula. Plate made twenty-four hours after barium meal. Note that the diverticula are definitely localized at junction of descending colon and sigmoid *A* and *B*. There is narrowing of the lumen of the colon from inflammatory tissue and spasm. Class II.

tiating this from the preceding group is a beginning narrowing of the lumen of the intestine. The apparent narrowing may at first be wholly due to spasm. It is usually best observed following the barium meal. Frequently the enema fails to reveal this spastic condition. In later cases, where there is actual thickening about the colon wall, the narrowing is constant both with the meal and enema.

Fig. 267.—Multiple diverticula. Condition similar to Fig. 266. Class II.

Fig. 268.—Multiple diverticula with beginning narrowing of the colon at *A*. Plate made following the barium enema. Rather diffuse distribution of the diverticula throughout the descending colon and sigmoid. Class II.

Under the fluoroscopic screen there is usually found localized tenderness. The sigmoid may be fixed from inflammatory adhesions. The infiltration of chronic inflammatory tissue in and about the intestinal wall will produce a demonstrable rigidity of the wall.

The condition which it is important to differentiate from cases

Fig. 269.—Multiple diverticula. Plate made after barium enema. Localized diverticula at *A*, with narrowing of the lumen mainly due to spasm. Phleboliths at *B* might be confused with diverticula, unless their presence had been previously recognized in the "preliminary examination."

in this group and the third group is *carcinoma*. I do not believe that a positive differentiation can always be made with the *x*-ray alone, particularly as a certain number of cases have malignant disease developing on top of a chronic diverticulitis. The history and physical examination as well as laboratory findings are of the utmost importance in making this differentia-

tion. In studying the *x*-ray plates there are one or two points which one must bear in mind when considering the possibility of cancer or diverticulitis.

In the first place, the *x*-ray appearance of diverticulitis tends to remain constant even over long periods of time. If malignant disease is present, repeated examinations show a progress-

Fig. 270.—Multiple diverticula. Plate made after the barium meal. Isolated diverticula at *A* and *B*. Secondary inflammatory changes involving descending colon. Class II.

ing lesion. If in a continued study of a diverticulitis case we find a portion of the involved area beginning to change its contour, one must be suspicious of a beginning malignancy.

Cancer, in general, is an intra-intestinal growth. The growth is in the wall of the colon, extending into the lumen and definitely circumscribed. The tumor mass in diverticulitis is out-

side the intestinal wall, being a pericolitis or perisigmoiditis. It is not definitely circumscribed.

Hence when we find a filling defect in the colon producing a narrowing of the lumen, with the transition from normal bowel to diseased bowel, immediately we suspect cancer. With a narrowing due to diverticulitis several inches of colon on either side of the actual point of narrowing will show more or less

Fig. 271.—Localized diverticula formation. Plate made after barium enema. Two diverticula at *A* and *B*. Narrowing of the colon at this point. Symptoms of chronic obstruction. Class II.

evidence of disease. In other words, in diverticulitis the transition from normal bowel to diseased bowel is *gradual*, while in cancer the transition is abrupt (Figs. 273 and 279).

Obstruction from cancer is likely to be severe, rapidly progressive, and finally complete. Obstruction from chronic diverticulitis is usually not severe, with a very gradual progress extending sometimes over a period of years, and rarely complete (Figs. 278 and 280).

Under the fluoroscopic screen an intermittent palpable tumor of the colon is always peridiverticulitis. A constant and persistant tumor mass may be cancer.

Group 3.—In the third group we put the cases showing advanced secondary changes associated with moderate to severe symptoms. In this group are the various forms of obstruction.

Fig. 272.—Diverticula at *A* and *B*, with narrowing of the colon at *B*. Barium enema. Class II.

The tendency in any chronic inflammatory mass is to contract. As we find a chronic obstruction following an indurated ulcer at the pylorus of the stomach, so with the inflammatory condition about the colon the same process takes place. The tendency in chronic diverticulitis is toward chronic obstruction, possibly extending over years.

Fig. 273.—Diverticula with advanced inflammatory changes. Plates taken following the barium enema. Infiltration of intestinal wall from *A* to *B*. One large diverticulum at *C*. Symptoms of obstruction. Operation showed a chronic inflammatory mass. Class III.

Fig. 274.—Diverticula with advanced inflammatory changes. Condition similar to Fig. 273. Class III.

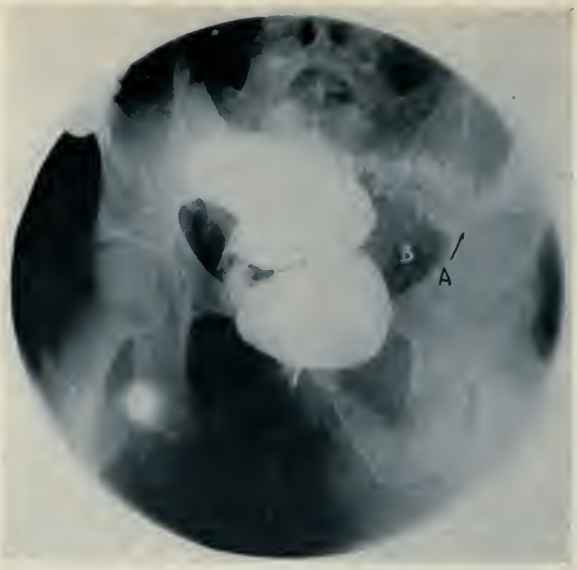

Fig. 275.—Multiple diverticula with chronic inflammatory changes. Plate taken after a barium enema. Narrowing of intestine from *A* to *B*. Operation showed tumor mass composed of chronic inflammatory tissue. Class III.

Fig. 276.—Chronic inflammatory changes involving descending colon and sigmoid. No diverticula are seen, but the intestine presents a serrated appearance such as is found associated with diverticulitis. Class III.

Fig. 277.—Chronic inflammatory changes about the descending colon and sigmoid. Plate taken after a barium enema. The "serrated" appearance is more marked than in the previous illustration. The individual diverticula are not seen. Class III.

Fig. 278.—Same case as Fig. 277, showing constriction at point *A*. Operation showed this to be chronic inflammatory tissue.

The *x*-ray picture of colon obstruction is characteristic and needs no special comment. There is stasis proximal to the point of obstruction with possible dilatation of this portion of the intestine. This is studied best following the barium meal. Plates should be taken at sufficient intervals to determine the

Fig. 279.—Cancer of the colon at point *A*; *B*, transverse colon; *C*, hepatic flexure; *D*, appendix. Plate taken after barium enema. Note the abrupt transition from normal bowel to diseased bowel, which is characteristic of growth. In Fig. 278 note that the transition from normal to diseased bowel is gradual. This is characteristic of chronic inflammation.

degree of obstruction—forty-eight or seventy-two hours after the meal, if necessary. The barium enema will confirm the meal and also give more detailed evidence as to the amount of colon involved and the degree of narrowing.

In this connection one must mention an appearance of the

Fig. 280.—Chronic obstruction from diverticulitis. Lesion at points *A* and *B*.

Fig. 281.—Same case as Fig. 280 four years later, showing complete obstruction to barium enema. Operation revealed chronic inflammatory mass.

colon which has become to our mind almost pathognomonic of chronic diverticulitis, although the diverticula themselves are not visualized. Particularly along the descending colon and sigmoid one occasionally finds a peculiar serrated appearance of the colon (Fig. 276). This may extend over several inches of the gut, and is associated with more or less narrowing of the lumen. These serrations are small, close together, and with a rather sharp point, presenting at times a saw-tooth appearance.

Fig. 282.—Drawing of specimen taken from preceding case. Shows cross-section of sigmoid, the wall of which is enormously thickened by chronic inflammatory tissue. Within the mass are seen the diverticula, to which the arrows are pointing. No evidence of malignancy.

They will not be confused with haustral shadows, for they are too numerous and too small, and, more important, they are constant in shape and position.

This serrated appearance is best seen following the enema, although it may be observed in the twenty-four-hour plate after the meal. Repeated enemata given on different days show this appearance to be constant.

The serrations do not change in size or shape. Further-

more, palpation under the fluoroscopic screen usually shows us that the intestine is more or less like a rigid tube. The walls are thickened and have lost their normal flexibility.

One infers that the serrated appearance is due to inflammatory thickening and induration in and about the intestinal wall, secondary to the presence of diverticula. The diverticula themselves not being visible, perhaps obliterated by the connective-tissue formation, or already so filled with mucus and fecal material that the barium is unable to enter.

There are other complications secondary to diverticulitis besides simple obstruction. Adhesions arising from the localized diverticulitis may involve other coils of intestines or other organs. Such a condition is best observed under the fluoroscopic screen.

Chronic perforation with abscess formation is not an uncommon sequel. The x-ray appearance is no different from a chronic perforation of gastric or duodenal ulcer. The plate may show an abscess cavity filled with barium outside the lumen of the gut, with a small isthmus of barium connecting it with the intestine. Acute perforations do not come to the x-ray man.

Some of the acute diverticulitis attacks simulate a left-sided appendix. The barium enema may be of help in such cases by demonstrating that the cecum and appendix are in normal position on the right side.

Rarely fistulæ may result from diverticulitis. Several cases have been reported of fistulæ connecting the bladder with the colon. Such conditions would be clearly shown on the x-ray plate.

In general, it must be borne in mind that the diagnosis of multiple diverticulitis is not to be made from the x-ray alone, although in some cases it may seem possible. The x-ray evidence must be considered in conjunction with the history, physical examination, and other laboratory findings. This is of particular importance in the differentiation of cancer and multiple diverticulitis.

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SOME FALLACIES IN THE DIAGNOSIS OF "PTOMAIN POISONING"

THE term "ptomain poisoning" has become both popular and vague. Jordan aptly states that it is a convenient refuge from etiologic uncertainty. In Europe the diagnosis of "ptomain poisoning" is seldom made, and the use of the term in any connection is very rare and quite guarded. In this country, however, cases of "ptomain poisoning" are still described in the medical journals, but more frequently in the lay press. Any acute gastro-intestinal attack resulting from a great variety of causes is apt to be called "ptomain poisoning." The diagnosis has fallen into disrepute because it lacks precision and has become a cloak for ignorance.

Selmi, in 1873, first used the word ptomain (from *ptoma*, a corpse) to include the poisonous products of putrefaction which gave the reaction then looked upon as characteristic of vegetable alkaloids. From the time of Selmi, when ptomains were regarded as animal alkaloids, our conception of these substances has changed markedly. The last attempt to give precision to the term was by Vaughan, who defined ptomains as intermediate cleavage products of protein decomposition.

For the past two years I have had charge of an investigation on the subject of "ptomain poisoning," in which I have been ably assisted by my associates in the Department of Preventive Medicine and Hygiene at the Harvard Medical School, especially by Professor J. Bronfenbrenner, Dr. D. L. Sisco, Dr. R. M. Atwater, Dr. John Weinzirl, Dr. E. W. Cheyney, Dr. W. G. Webber, Mr. M. J. Schlesinger, Mr. P. F. Orr, Miss C. R.

Davis, Miss H. Husted, Miss E. Wolff, and a group of others working upon the chemistry, bacteriology, and epidemiology of the subject of food poisoning. During the course of this investigation a special effort was made to discover and study every case occurring in and around Boston. As a result of these studies a number of interesting facts were discovered, which will form the basis of an extensive report. Here I want to call attention to some curious fallacies in the diagnosis of "ptomain poisoning." A careful study disclosed the fact that some of the cases were bacterial infections, others were caused by corrosive or irritating chemical substances, and still others were much wider from the mark.

We have searched in vain for "ptomains" that might cause gastro-intestinal or other symptoms. Split products of protein putrefaction are readily isolated. Some of these products have physiologic activity, but none of them so far have been demonstrated to be poisonous when taken by the mouth. The so-called ptomains isolated and described by Selmi, Nencki, Breiger, Schmiederberg, Faust, and Vaughan were usually obtained from putrid organic matter that had decomposed past the point where it would be used as food. Furthermore, most of these substances were tested by injecting them subcutaneously or intravenously into animals. Many substances are poisonous when thus introduced parenterally, although they may be harmless by the mouth. Again, many of the so-called ptomains isolated and described have since been shown to contain impurities. Chemists are now seldom confident of the purity of protein fractions, even when obtained in crystalline form. The chemical search for split protein products as the cause of "ptomain poisoning" has practically been abandoned. Most of these split products are amins, which are either not poisonous at all, or no more so than their corresponding ammonia salts. The chemical resemblance between muscarin and cholin has directed the work toward the phosphatids, but thus far this line of research has not helped solve the puzzle of "ptomain poisoning."

I have selected some instructive cases illustrating fallacies in the diagnosis of "ptomain poisoning" which have come to

our notice during the past two years in the investigations which we are carrying on at Harvard. Most of the following cases we have investigated personally; information concerning some of them was obtained by correspondence or from the literature.

Oxalic Acid Poisoning.—Our case No. 1, A. V. D., female, age fifty-eight. Ate about a half-peck of cooked rhubarb leaves (tops) Monday, May 14, 1917, at 4 P. M. Also took much of the water in which the leaves were cooked. Patient was sick all night; started to vomit about 3 A. M. on the morning of the 15th. At the same time diarrhea commenced and continued during the night, but bowels did not move again until the time of death. Patient vomited throughout the entire illness, was very thirsty, and drank a great deal of water. Temperature normal. Patient had had chronic pains in abdomen for many years, which were much intensified during this period. Died in ten days. Rigor mortis did not set in until thirty hours after death. Bacteriologic examination of material obtained post-mortem by rectal swab showed that the case was complicated with dysentery.

A brother-in-law of the patient ate some of the greens and was sick all night, but recovered. A sister of the patient ate a very small amount of the greens, and had but slight malaise.

Diagnosis: Oxalic acid poisoning. This case was investigated by us because it was reported as "ptomain poisoning."

A similar instance was reported in the Weekly Bulletin of the New York City Department of Health September 16, 1916. This was suspected "ptomain poisoning" due to sour-grass soup. The report follows:

"Some time ago, through our Weekly Bulletin, we asked physicians to be on the lookout for cases of ptomain poisoning, and to promptly report all such cases to the Department of Health. On investigation, very few of the cases proved to be really ptomain poisoning.

"A recent investigation showed that several cases of illness occurring in the East Side and originally thought to be due to ptomain poisoning were really due to sour-grass soup. The soup was prepared from 'Qchav' or 'Szchav' leaves, more commonly

known as sour-grass—a species of sorrel. This plant is rich in oxalic acid salts, analysis in the Health Department's chemical laboratory showing as much as 2 grains of oxalic acid in 1 ounce of the leaves, and double that in the stems.

"An inspector of the Health Department's Bureau of Food and Drugs found that sour-grass soup is a common dish in some of the East Side restaurants. In some cases the stalks of the leaves are discarded as too acid. In one restaurant the inspector found that the stalks were removed, the leaves then well washed, and the washings rejected. After that the leaves were soaked in cold water overnight and then boiled in water for fifteen minutes. This extract was poured off and rejected. A second boiling of the leaves then followed, after which eggs and cream were added. The dish was then ready to serve. Chemical analysis of the finished soup showed about *10 grains of oxalic acid per pint of soup.*"

Belonging to this group of irritating chemical substances is the following account which we obtained from Chicago:

Tartar Emetic.—During the summer of 1917 a number of cases of "ptomain poisoning" occurred in Chicago due to tartar emetic. This drug was given to guests in hotel dining-rooms and restaurants who had slighted waiters in giving "tips." Ten waiters were indicted by the Grand Jury. The Assistant States Attorney wrote me as follows: "That 'Micky Finn' powders were given to guests at banquets and in hotels and restaurants is well established by the evidence in possession of this office. The analysis shows the powder to be pure salt of antimony and potassium nitrate, known by the trade as tartar emetic."

Saltpeter.—Our case No. 5. This was an outbreak of diarrhea occurring during June and July, 1917, in the 6th Massachusetts Regiment, at Camp Darling, Framingham, Mass. We were asked to investigate a small outbreak of diarrhea at the camp, and I sent Dr. Atwater there on July 9, 1917. The symptoms were mild and without fever. A study was made of the blood and feces and also of the food, milk, and water. Nothing indicative was discovered chemically or bacteriologically. Suspicion was then aroused toward some mischief maker with

malicious intent. Finally, an old Navy surgeon suggested looking into the sugar. It was found to be somewhat unusual in taste. Dr. Webber found a sample of this sugar to contain about 1 per cent. of potassium nitrate. It is assumed that the saltpeter was added to the sugar as an anaphrodisiac. This ineffectual attempt at chemical morality cannot meet with the approval of the true reformer. The sugar was changed and the trouble ceased.

Uremia and Neoplasm.—Our case No. 56. This illustrates loosely and vaguely the term "ptomain poisoning" is used even in one of our best and oldest medical journals. The following editorial appeared in the Boston Medical and Surgical Journal of February 13, 1919, p. 204:

"Dr. Thomas F. Harrington, Deputy Commissioner of the State Board of Labor and Industries, died at his home in Boston, January 19, 1919, after a five weeks' illness from ptomain poisoning."

Investigations made by Dr. Sisco disclosed the fact that Dr. Harrington thought he was troubled with "ptomain poisoning," and this must have been the origin of the diagnosis. The true facts appeared in an editorial correction in the Boston Medical and Surgical Journal of April 3, 1919, p. 398:

"In a recent issue of this Journal was published an obituary of Dr. Thomas F. Harrington in which it was said that the cause of his death was "ptomain poisoning." Further investigation of this diagnosis, with the physician in attendance upon Dr. Harrington and the death certificate, has disclosed, first, that the origin of the diagnosis is unknown, and second, that the immediate cause of death was uremia, an apparent result of a neoplasm which obstructed the ureters."

The report of Dr. Harrington's last illness is a very good illustration to show how deep-rooted the fallacy of "ptomain poisoning" has grown, and how loosely the term is used.

In the Journal of the American Medical Association, March 17, 1917, one of the causes of chronic nephritis is given as "repeated ptomain poisoning."

Dysentery.—Our case No. 52. One of the early instances

of "ptomain poisoning" investigated by us was a family outbreak which turned out to be bacillary dysentery. The following is a condensed account of the essential features:

Wood family consisted of mother, father, and four children, all living in Avon, Mass. On August 23, 1918, the entire family went to visit the wife's parents at Randolph. On the 27th the baby was taken sick, having malaise, diarrhea, and fever as the chief symptoms. The child tossed its head about a great deal during its sickness. No blood was noticed in the stools. Child died on September 1st. No autopsy was done.

On the 26th of August Gladys (nine years old) had abdominal pains and a profuse diarrhea with movements every fifteen minutes. The stools were bloody and contained mucus. Later there was vomiting and fever. Child was sick until September 3d.

On September 1st Thirza (three years old) began to have a bloody diarrhea with fever. There was also a twitching and tossing of the head. She died September 9th, having vomited the morning death took place.

On September 3d Thelma (seven years old) developed bloody diarrhea, which did not last very long.

Mother and father each had a slight attack of diarrhea, but not of long duration or great intensity. Same was true of the grandparents.

Investigation of diet showed that meat and salt fish had been brought with the family from Avon, but that otherwise food eaten was purchased in Randolph. Family suspected overripe cantaloup, but no evidence was found to support this.

It was found that there had been a number of such cases of sickness in Randolph and several deaths.

An autopsy was performed on Thirza Wood, and an account of the findings disclosed lesions of bacillary dysentery. Bacteriologic examination of the intestines gave a positive culture of the dysentery bacillus (Shiga).

Bacterial Infections.—We now know that most of the cases formerly called "ptomain poisoning" are, in fact, instances of bacterial infections. It is not even proper to call such cases

food poisoning. No one would think of speaking of a case of typhoid fever contracted from milk as food poisoning. There is in this category a group of gastro-intestinal disturbances caused by the *Bacillus enteritidis* and its congeners. Gärtner, 1888, described an outbreak associated with the *Bacillus enteritidis* which has since been called the Gärtner bacillus. This micro-organism belongs to the colon-typhoid group, and is the type of a number of closely associated, Gram-negative, spore-free bacilli which have a certain amount of pathogenic power. They are taken into the system with food and drink; direct and indirect infection occurs; food, fingers, and flies play a rôle in the transfer of these infections, as they do in the case of typhoid fever. Bacillus carriers of this group are suspected, but are probably rare. Infections of this type bear a close resemblance to paratyphoid fever. They are much more common abroad than in this country; at least, they are reported much more often from England, Germany, and France. These outbreaks are very apt to be associated with church suppers, sorority picnics, and fraternity dinners. The reasons seem self-evident when we investigate the way the food is often prepared, handled, kept, and served at such functions. It is no longer the fashion to call bacterial infections belonging to this class "ptomain poisoning," for they have a distinct etiologic standing of their own. We are making an extended study of this phase of the subject, and will have a report upon it at a later time.

Indigestion.—Our case No. 8, M. J. R., male, forty-nine years, played golf on July 23, 1917, a particularly warm and humid day. While fatigued and overheated ate an ear of boiled green corn, ham omelet, cold slaw with mayonnaise, potatoes, watermelon, and cake. During the night had abdominal pain in region of the umbilicus. At daybreak took a Seidlitz powder, and this was followed by two or three loose semiformed movements, not noticed to contain blood or mucus. Felt weak and tired; no nausea, no vomiting, but a slight headache added to the effect of the malaise.

Temperature next morning, July 24th, 101° F. Entered hospital about noon. On admission, pulse 100, temperature

100.6° F. Was given calomel, six doses of 10 milligrams each, at fifteen-minute intervals. The temperature rose to 101.2° F. that evening, but the next morning was 99° F., and later the same day returned to 98.6° F. and remained normal. No further symptoms.

White cell count was 5200. Stools contained Bacillus coli and B. coli communior, but no pathogenic bacteria.

The diagnosis was doubtless a mild heat exhaustion, accentuated by acute indigestion due to indiscretion in diet, and, furthermore, eating too quickly while fatigued and overheated.

Acute digestive troubles with a great variety of symptoms and from a great variety of causes are often loosely and carelessly called "ptomain poisoning."

Nervous Diarrhea.—Our case No. 10. On March 15, 1918, Dr. X. ate some experimental food at a luncheon club, which is maintained at the Department of Preventive Medicine at the Harvard Medical School for the express purpose of studying the problems in question. Fifteen minutes later Dr. X. became very nervous and worried about his condition, questioning the other men in the laboratory concerning his appearance, etc., and watching himself closely for symptoms of illness. His apprehension about himself was accentuated by injudicious teasing on the part of his colleagues. Within about two hours he developed a moderate diarrhea which lasted for several hours. There were no other symptoms.

The experimental food was canned corn, and was eaten by three other individuals, none of whom complained of illness. The analysis of these cans by Dr. Weinzirl revealed no organisms. Dr. X.'s dietary for the preceding five days contained nothing which would be looked upon with suspicion.

His diarrhea was doubtless of "nervous" origin, especially as he gave a history of similar attacks brought on by emotion or excitement.

Botulism.—Recently three deaths occurred in Spokane, Washington, which were reported as due to "ptomain poisoning." Upon investigation they were shown to be botulism, said to be due to home-processed beets.

Botulism is a true toxemia. It is caused by a toxin which is produced by the Bacillus botulinus in nitrogenous food. The toxin is produced at room temperature in vegetables and fruits as well as in sausage and other meats. It has a striking symptomatology and is often fatal, but is a very rare cause of food poisoning. Botulinus poison is a true toxin, and corresponds in all essential respects to the toxin of diphtheria and the toxin of tetanus, the only difference being that it is poisonous when taken by the mouth, whereas the toxins of diphtheria and tetanus are only poisonous when injected into the tissues. It is just as irrational to call botulism "ptomain poinsoing" as it would be to call diphtheria or tetanus by this name.

Anaphylaxis.—Anaphylactic reactions to certain foods are of very common occurrence. These reactions are sometimes severe and are accompanied by urticarial eruptions of the mucous membrane as well as of the skin. These changes may take place in the esophagus and perhaps the stomach, for it is not uncommon to have vomiting in severe cases, and the vomitus sometimes contains blood. The attacks are usually severe and come on suddenly, and in a number of instances have been mistaken for "ptomain poisoning." Persons who are hypersusceptible to certain foods, such as shell-fish, strawberries, etc., sometimes associate these symptoms, and the literature contains a number of instances of this condition being mistaken for "ptomain poisoning."

Oxalic acid, tartar emetic, and saltpeter; uremia and cancer; dysentery and bacterial infections; indigestion, nervous diarrhea, botulism, and anaphylaxis have all been mistaken for "ptomain poisoning." It is not necessary to give further instances showing the fallacies in this diagnosis. The term should be avoided, for it lacks precision. In fact, "ptomain" is a term for a chemical substance of uncertain origin, unknown nature, and doubtful existence.

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CLINIC OF DR. LEWELLYS F. BARKER

JOHNS HOPKINS HOSPITAL

FUNICULAR MYELITIS, OR COMBINED SCLEROSIS OF THE SPINAL CORD

March 4, 1919.

WE have today an interesting case illustrating the condition known in this country as *combined sclerosis of the posterior and lateral funiculi*, or *funicular myelitis*.

Changes in the white columns of the spinal cord associated with varying degrees of anemia were first investigated in Europe by Lichtheim and his student, Minnich, between the years 1887 and 1891; and in the United States by J. J. Putnam in 1891. Nonne in 1893 attempted to separate such conditions from others in which anemia is not present or is only slight. He believed that myelitic conditions associated with anemia could be divided into two groups, in one of which pernicious anemia was the primary disease, the changes in the spinal cord being entirely secondary to it, whereas, in the other, any anemia present was secondary to the changes in the spinal cord. As opportunity for observation increased, the difficulty of keeping these two groups separate became more and more evident, and the view was soon advanced that there is really no essential difference between them. This opinion was supported by Nonne in his later contributions to the subject. In 1895 Rothman described a series of cases in which he assumed that the ganglion cells were the seat of the primary disease, degeneration of the nerve-

fibers following as a secondary phenomenon. This condition he proposed to separate from other forms of myelitic spinal disease on the ground that it is a disease *sui generis*. Five years later an article appeared by the English observers, Russell, Batten, and Collier, containing a description of the same class of cases, together with evidence pointing to associations with a toxin that causes more or less injury to the blood-making organs. In the United States, besides the important early articles of J. J. Putnam and C. L. Dana, excellent papers on the subject have been published by Taylor and Waterman, by Barr and McCarthy, by Billings, by Grinker, and by Camac amd Milne. The opinion that there is no essential distinction between so-called "pernicious anemia accompanied by changes in the spinal cord" and "combined sclerosis of the cord accompanied by anemia" has been steadily gaining ground, and is now generally accepted. The difference between the two groups of cases lies in the fact that in some persons the anemic changes make their appearance earlier and are more severe than those in the spinal cord, whereas in other persons these conditions are reversed. The patient before us this morning is an interesting example of the second type, namely, that in which the symptoms indicate that the cord changes are definitely established, though the blood changes have only begun to appear.

The patient, C. E. C., is a married man, forty-five years old. He was admitted to the hospital less than a week ago, complaining of inability to walk and of a sense of constriction at the waist, as though a bandage were tied around it. His family history contains nothing bearing upon his present illness and his past history is unimportant except for the fact that he had a Neisserian infection about twenty years ago. When you hear of inability to walk, accompanied by a binding sensation around the waist, what system would seem to you to be involved?

STUDENT: The nervous system.

DR. BARKER: Yes. Now in studying conditions associated with the nervous system we follow certain rules. In the diagnosis of such affections, we pass through three stages. First of all, we accumulate the data; second, we try to make a topo-

graphic diagnosis, if possible, of the changes taking place in the nervous system, that is, we determine the locality of the lesion or lesions; third, having localized the lesions, we proceed to ascertain their nature. We shall begin here, therefore, by collecting the necessary data.

The patient's present illness began about a year ago, when he noticed a slight numbness in the fingers of both hands, most marked in the middle fingers. (To patient): Were you quite well up to that time?

PATIENT: Yes.

DR. BARKER: About two weeks later he noticed a similar sensation in his toes, the numbness being succeeded by a feeling of coldness. This numbness in the toes gradually extended up the legs, until, in about three months, it reached the waist; at this time the patient began to experience also the sense of constriction already mentioned. There was no extension of the numbness in the upper extremities; progress in the numbness was entirely confined to the lower part of the body. As the numbness increased the patient began to feel weak in the legs, soon after which he began to limp on the right side. About three months ago he recognized that he could not control the escape of gas from the rectum. Has there been any incontinence of urine?

STUDENT: No, but he says he sometimes has trouble in starting the flow.

DR. BARKER: The weakness in the lower extremities has grown gradually worse, until now he is practically unable to walk at all. Some time ago he noticed that when he stood up with his eyes closed he was in danger of falling. Since the onset of his illness he has been depressed, and he states that he is emotionally upset more easily than formerly. In other respects the symptoms have remained unchanged. (To patient): How long is it since you were obliged to give up walking?

PATIENT: About five weeks.

DR. BARKER: These are all the positive data in the anamnesis bearing upon the diagnosis. (To patient): Have you had headaches?

PATIENT: No.

DR. BARKER: Any dizziness?

PATIENT: Only since I have been in the hospital.

DR. BARKER: Any ringing in your ears?

PATIENT: No.

DR. BARKER: Any cough?

PATIENT: No.

DR. BARKER: Any shortness of breath?

PATIENT: No.

DR. BARKER: Any palpitation of the heart? Does your heart ever beat fast?

PATIENT: No.

DR. BARKER: Have you a good appetite?

PATIENT: Yes.

DR. BARKER: Is there ever any gas coming from the stomach?

PATIENT: Sometimes.

DR. BARKER: Do you ever have any nausea or vomiting?

PATIENT: Occasionally.

DR. BARKER: Are your bowels regular? Have you any constipation or diarrhea?

PATIENT: I was constipated sometimes when I was up and about, and it has been worse since I have been in bed.

DR. BARKER: Have you any trouble from hemorrhoids or piles?

PATIENT: A little, sometimes.

DR. BARKER: Is there ever any bleeding?

PATIENT: No.

DR. BARKER: No bleeding hemorrhoids. (To student): Have you anything of importance to report about the patient's habits?

STUDENT: He has never been employed in manual labor. For the last three years he has been a watchman and before that he was in a mercantile business.

DR. BARKER: How about potatorium? (To patient): Do you ever drink anything?

PATIENT: For fifteen or twenty years I used to drink three or four glasses of beer a day, but I have given it up now. I have never drunk whisky and I have never smoked.

DR. BARKER: Has he had any infections?

STUDENT: About twelve years ago he was in bed for a week with what was called "typhomalaria."

DR. BARKER: It may have been malaria. It could hardly have been typhoid unless it were a very mild attack. Has he ever been operated upon?

STUDENT: No.

DR. BARKER: Is there any history of trauma?

STUDENT: No.

DR. BARKER: So much for the anamnesis. Examination on admission to the dispensary was negative except on the neurologic side. How about his teeth? There is some pyorrhea. Are there any dead teeth?

PATIENT: I have had several teeth extracted. I think they were dead.

DR. BARKER: Open your mouth, please. Yes, there are still several teeth with large fillings present and others that look discolored. Probably there are still some dead teeth here, but no *x*-rays have been taken as yet, as he has been here only a few days and has not yet been down to the dental clinic. Examination of the head was negative, was it not?

STUDENT: Yes.

DR. BARKER: There is no struma; the neck is negative. The heart and lungs are negative. Abdominal palpation was not wholly satisfactory, because the abdomen was held so rigidly.

Let us begin our objective study of his nervous functions by examination of the motility. Here we find considerable weakness, especially in the legs, and some spasticity. (To patient): Bend your right leg, please. Is that all you can do? Now use your full strength and try to prevent me from bending your knee. He has but little power in the muscles of this leg. Let us try the left leg in the same way. You see there is about the same condition of things as in the right leg. Both the flexors and extensors are evidently weak. (To patient): Now shove down as hard as you can. Do it again, please. Now the other foot. You can see the evidence of weakness plainly

on both sides, but it is greater on the left side. (To patient): Now I want you to make a circle in the air with your right foot. It is a question, at first, whether the tremulous, indefinite movements he makes are due to weakness or to ataxia. (To patient): That's better. Now try to do it with the left foot. As hard as you can. I am trying to prevent you and I want you to resist me. All the muscles of the lower extremities are obviously weak.

Now let us test the muscles in the upper extremities. (To patient): Grip my hand with your own right hand, please. As hard as you can. Now with your left hand. His grip is very poor on both sides. (To patient): Pull my hand as hard as you can. Now shove it. Now do the same thing with your left arm. The flexors and extensors of the elbow seem to be fairly strong.

Next we will test the abdominal muscles. First of all, we will ascertain the presence or absence of Beevor's sign. According to Beevor, if there is any paralysis of the lower segment of the recti muscles, there is a riding up of the umbilicus when the patient tries to raise his head and sit upright. (To patient): Sit up, please. No, try again without using your arms. Fold them across your chest. There is certainly no outspoken paralysis of the abdominal muscles and Beevor's sign is not present. The abdominal muscles may be a little weak, but we must bear in mind that he has not used them for some time.

Now let us test the muscles of the head and neck. (To patient): Wrinkle your forehead. Frown. Show your teeth, please. The muscles innervated by the seventh nerve contract well. Close your jaws tightly together as though biting hard. His masseters contract strongly. What nerve did I test then?

STUDENT: The motor branch of the fifth nerve.

DR. BARKER: Yes. The masseter muscles are supplied by the mandibular branch of the fifth. (To patient): Look at my finger, please. Look at it as I move it from side to side. Look up. Look down. The eye muscles work well. There is a slight von Graefe's sign and a slight Dalrymple sign, but neither of these is well marked. There seems to be nothing

wrong then with the third, fourth, and sixth cerebral nerves. We have tested the motor part of the fifth and the seventh. (To patient): Can you swallow without difficulty?

PATIENT: Oh, yes.

DR. BARKER: The ninth and tenth nerves seem to be working satisfactorily.

Can you tell me the name of the eleventh cerebral nerve?

STUDENT: The *nervus accessorius.*

DR. BARKER: Yes. How would you proceed to test it?

STUDENT: I am afraid I don't know.

DR. BARKER: What muscles does it supply?

STUDENT: The sternocleidomastoid muscle and the upper part of the trapezius.

DR. BARKER: Yes. Then we can determine its condition most easily by testing the activity of the sternocleidomastoid. (To patient): Turn your head to the left, please. Now to the right. You see, there is no paralysis. Now let us test the twelfth nerve, that is, the hypoglossal or motor nerve of the tongue. (To patient): Put out your tongue, please. You see there is no difficulty there—no paralysis of the hypoglossus.

That concludes our examination of the motor activities of the cerebral nerves. Has the patient's sensation been tested? We shall leave the reflexes until a little later. What was found as regards sensation on examination in the ward?

STUDENT: Rough tests of sensation showed impairment of the tactile sense on the medial surfaces of the lower extremities just below the knee and also on the dorsum of the foot.

DR. BARKER: You found a little loss of tactile sensibility, then?

STUDENT: Not very much.

DR. BARKER: Let us try for ourselves. I shall stimulate with a camel's-hair brush. (To patient): Now close your eyes, please, and tell me whenever you feel the slightest touch.

Notice how good his power of attention is. As I test below the knee, he recognizes every touch immediately. (To patient): Close your eyes again, please, and tell me at once if I touch you. You perceive that in this investigation I am purposely varying

the tempo of the stimulation intervals. Certainly, at present, he recognizes every stimulus promptly as far as touch is concerned. The only evidence of impaired sensation that he has shown in the ward is a slight dulling of perception on the inner surface of the thighs. Now let us test for sensations of heat and cold. (To patient): Close your eyes, please, and tell me whether you feel something warm or cold. As you see, I am testing very roughly. He recognizes warmth correctly every time. His recognition of cold is not quite so acute, but it is possible that the perception of cold may be confused with that of touch because the breath stirs the hairs on the surface of the extremities and so stimulates the sense of touch. Did you notice any disturbance of temperature-sense in the ward?

STUDENT: No.

DR. BARKER: How about pain?

STUDENT: No analgesia was made out.

DR. BARKER: Let us try for ourselves with a pin. (To patient): Tell me when you feel the point of the pin, but when you feel the head of the pin do not say anything.

PATIENT: Now. Now. Now.

DR. BARKER: You see he recognizes the prick of a pin everywhere. Now let us find out if there is any bathyanesthesia. Bathyanesthesia is a term covering the loss of deep sensibility. When this is lost or diminished we have to do not only with a loss of sensibility as such, but with a loss of the unconscious centripetal impulses that play an important part in the maintenance of muscular tonus and the co-ordination of muscular activity. (To patient): Close your eyes, please. Now tell me whether I am moving your great toe upward or downward?

PATIENT: I can feel you touch it, but I don't feel it move at all.

DR. BARKER: You can all of you see me move his toe passively. I would have you note that a patient whose nervous system is normal can distinguish the direction of any movement that you can see. (To patient): Let us try the other foot.

PATIENT: I can feel you touch it, but I can't tell whether you are moving it up or down.

DR. BARKER: There is plainly disturbance of position-sense and of the sense of passive movement in both great toes, indicating definite bathyanesthesia. Now let us apply the same test a little higher up. (To patient): As I bend your ankle, tell me whether I am moving the foot up or down?

PATIENT: I can't tell.

DR. BARKER: You could all, even those of you at a distance, see that I cause a considerable excursion of the foot, but the patient was not conscious of it. Now for the knee. In making this particular test you must take care that the leg is placed half-way between flexion and extension. (To patient): Close your eyes and tell me whether I bend your knee or straighten it.

PATIENT: I can't tell which.

DR. BARKER: Did I move it at all?

PATIENT: I can't say.

DR. BARKER: Now we will try the other knee. (To patient): Can you feel any movement now?

PATIENT: No; none at all.

DR. BARKER: This is a really striking example of bathyanesthesia. Though his knee is bent and straightened, he does not feel the changes. Now let us test the upper extremities. (To patient): Close your eyes, please, and tell me whether I am moving your hand up or down.

PATIENT: Now you are moving it upward. Now downward. Upward. Downward.

DR. BARKER: Here he recognizes passive movement and its direction promptly.

Next, we shall test the wrist. Then the elbow. You see that in each case, even with such a slight amount of excursion as I am making now, he recognizes the nature of the movement correctly. The bathyanesthesia seems, then, to be confined to the lower extremities.

Has there been any disturbance of the special senses?

STUDENT: No.

DR. BARKER: No optic atrophy or choked disk?

STUDENT: No. The disks are clearly outlined and there is no sign of atrophy.

DR. BARKER: How about his hearing?

STUDENT: Fifteen years ago he had an attack of earache in his right ear, and ever since then he has been slightly deaf on that side, but not much so.

DR. BARKER: Is his sense of smell all right?

STUDENT: Yes.

DR. BARKER: Taste also?

STUDENT: So far as we have yet observed.

DR. BARKER: The special senses will have to be tested more closely later on, but they seem to be quite normal as far as can be determined by a rough examination.

Now, we know that in this patient there is marked bathyanesthesia of the lower extremities, and if there is bathyanesthesia there should be something else also. (To patient): Close your eyes once more, please. Now put your right heel on your left knee. You see at once that he cannot make adequate measurements. There is hypermetria, that is to say, he overmeasures the distance to be covered. (To patient): Keep your eyes closed, please. Now I will put your right heel on your left knee, and I want you to run your foot steadily, straight down the shin. You see how his foot wanders in trying to accomplish this movement. Dynamic ataxia is well marked in the lower extremities. It is always present when there is bathyanesthesia, but this is a wonderful example of it. (To patient): Now raise your right foot 6 inches from the bed and hold it steadily in that position. This is the test for static ataxia.

PATIENT: I can't tell how far off my foot is from the bed.

DR. BARKER: You see that he cannot form any correct conception of distances. (To patient): Now I am going to raise your heel a foot from the bed and I want you to hold it steadily there. Is that a foot from the bed?

PATIENT: I can't tell.

DR. BARKER: You see he holds the foot with a fair degree of steadiness, though he has no conception of the distance from

the bed at which he is holding it. There is very little static ataxia, though the dynamic ataxia is well marked.

Now let us investigate the question of ataxia in the upper extremities. There was no bathyanesthesia of the arms; we shall probably find that there is little or no ataxia. (To patient): Close your eyes and touch your nose with the tip of your left forefinger, please. Now try the same thing with the other hand. You see he accomplishes this maneuver with fair success. There is only a slight miscalculation.

The whole state of things here is very interesting. There is good postural sense and passive motion in the arms, with very little ataxia. In the lower extremities conditions are exactly the reverse.

Now let us test for hypertonicity or hypotonicity of the muscles. (To patient): Let this leg go just as loose as possible, please. You see the minute I start to move that leg it goes into a condition of hypertonicity that interferes with passive motion. I would have you notice that we have here an unusual condition, in which there is loss of deep sensation, associated with hypertonicity. This is the opposite of what we should expect. In general, bathyanesthesia is associated with hypotonicity. You will recall the conditions in tabes dorsalis. In the upper extremities there is no bathyanesthesia and there is no hypertonicity.

Now we may proceed to test the reflexes. What did you find out about them in the ward?

STUDENT: There was a little hyperactivity of the deep reflexes.

DR. BARKER: Only a little? At this moment there is more than a little. At present there is, as you can see, an extreme degree of hyperactivity of the knee-jerks. You see an exquisite patellar clonus on both sides. The ankle-jerks also are hyperactive; it is rather difficult to test the ankle-jerks when the patient is lying in bed. Still, we can perceive that in this case there is marked exaggeration of the Achilles jerk. You will observe that the hypertonicity in the lower extremities is corroborated by the exaggerated reflexes, whereas in the upper

extremities, where there is no hypertonicity, the radial, the biceps, and the triceps reflexes are all about normal. Let us turn to the superficial reflexes. You see that the abdominal reflexes are present. In what disease are the abdominal reflexes usually absent on both sides?

STUDENT: In multiple sclerosis.

DR. BARKER: Yes. In this case, as you have seen, the abdominal reflexes are present, both above and below. When we try the plantar reflexes by tickling the soles of the feet we find that there is a positive Babinski in both feet, but it is accompanied by a marked tickle response. (To patient): Does that hurt you?

PATIENT: Yes indeed, it does.

DR. BARKER: You perceive it causes very evident suffering. Painful soles of the feet on stimulation is a neurologic phenomenon that is sometimes of diagnostic significance. In what condition do we find it. Can anyone answer?

STUDENT: In alcoholic polyneuritis.

DR. BARKER: Yes. Whenever you find the plantæ painful on testing for the plantar reflex you should always think of potatorium. The Gordon reflex is positive here. Oppenheim's sign is not easily elicited in this patient. There seem to be painful points along the peripheral nerves. This is important and the Valleix points should be carefully tested, because one of the features of alcoholic neuritis (pseudotabes) is the presence of such painful points. (To patient): You said you had been in the habit of drinking beer?

PATIENT: For fifteen or twenty years I drank three or four glasses of beer a day, but for the last two years I have taken very little.

DR. BARKER: Three or four glasses a day for fifteen or twenty years, though a mere drop compared with the amounts imbibed by some beer-drinkers, means, in the aggregate, a good deal of alcohol. Still, for two years he has been abstemious. Has the patient shown any hallucinations? Delusions? Depression? Disorientation?

STUDENT: No, nothing of the kind.

DR. BARKER: There is very little, then, in the history or in the results of the examination that points to disorder of the cerebral functions.

I think we have now collected the necessary data bearing on the nervous system, and we have spent a good deal of time in doing so. Now let us proceed to summarize our neurologic findings. (The patient at this point was taken back to the ward.)

We have inability to walk with pronounced paresis and ataxia of the lower extremities associated with hypertonicity of the muscles. In the upper extremities there is a little paresis without hypertonicity. The reflexes in the lower extremities are hyperactive, so much so that there is actual clonus. There is also marked bathyanesthesia of the lower extremities without surface anesthesia. There is very slight sphincter disturbance. The tactile perception seems nearly normal. Apparently there is no involvement of the cerebral nerves. The eyes seem normal. The pupils are equal. The Argyll Robertson pupil is not present. All the symptoms have come on rapidly, that is, within the last year. They include certain important subjective symptoms, namely, tingling sensations in the fingers and toes, extending up the lower extremities to the waist, where there is a sense of constriction. The important objective sensory finding is the bathyanesthesia associated with the marked dynamic ataxia of the lower extremities.

Let us endeavor now to localize the lesions. Do you think the condition functional or organic?

STUDENT: I think it is organic.

DR. BARKER: Yes; it must be organic. Next, is this organic disease situated in the cerebrospinal or in the sympathetic system?

STUDENT: I think in the cerebrospinal system.

DR. BARKER: Yes, as far as we have gone, everything points to the cerebrospinal nervous system. Now, is the brain the part of the nervous system that has been most affected, or has the part of the nervous system below the brain been more involved?

STUDENT: The part below the brain.

DR. BARKER: Yes, for there is no disturbance of the functions of the cerebral nerves, nor of the functions of the cerebrum and cerebellum. The eye-grounds are negative; there is no temporal pallor of the optic disks and no Argyll Robertson pupil. Everything seems to rule out the cerebrum.

If the organic nervous condition with which we are here dealing is below the brain, are we to think of it as being in the spinal cord itself or in the peripheral nerves? Before actually deciding this point I shall ask you to consider, since the head is free, what parts of the body below the head are chiefly affected.

STUDENT: The lower parts.

DR. BARKER: Yes. The symptoms are distinctly more marked below than above the level of the middle of the body. But the numbness of the fingers and the weakness in the hands shows that there is some involvement above the middle of the body as well.

The next point for us to consider is whether this condition is a spinal-cord or a peripheral affair. Let us take, first, the question of the disturbances of motility. Are they due to lesions of the upper or of the lower motor neurones? What do you think?

STUDENT: I should think the upper motor neurons.

DR. BARKER: Why?

STUDENT: From the fact that the reflexes are hyperactive, and besides there is a positive Babinski reflex on each side.

DR. BARKER: You are right. Such a spastic hyperactivity of the reflexes as we see here and the positive Babinski sign always point to lesions of the upper motor neurons. Now the upper motor neurons are situated entirely within the central nervous system. They do not enter the peripheral nerves. Let us recall the histology of the upper motor neurons. Where are the cell bodies belonging to the upper motor neurons situated?

STUDENT: In the motor area of the cerebral cortex.

DR. BARKER: Yes; chiefly in the anterior central gyrus and in the paracentral lobule. Describe, please, the course followed

by the axones that are given off by the cell bodies of these upper motor neurons.

STUDENT: They traverse the centrum semiovale, pass through the internal capsule and the foot of the cerebral peduncle, and enter the brain-stem; having gone through the basilar part of the pons, they form the pyramids of the medulla; most of the fibers of the pyramids undergo decussation in the medulla oblongata, the crossed fibers passing down to form the lateral pyramidal tract of the spinal cord, the uncrossed fibers going to form the direct pyramidal tract of the anterior funiculi. All these axones end in arborizations about the cell bodies and dendrites of the anterior horn cells in the gray matter of the spinal cord, thus synapsing with the lower motor neurons.

Could the pyramidal tract be affected from the cortex?

STUDENT: I think it could.

DR. BARKER: Yes, it could be. If the cell bodies were injured, the secondary degeneration would extend to the spinal cord. But if the lesion were situated there, we should expect to have some evidence pointing to disturbed functions of the upper motor neurons that synapse with the lower motor neurons of the cerebral nerves. Could the pyramidal tract be injured below the head—say, in the spinal cord itself? If so, would the lesion be in the anterior funiculi, the posterior funiculi, or in the lateral funiculi?

STUDENT: In the anterior funiculi for the uncrossed pyramidal tracts and in the lateral funiculi for the crossed tracts.

DR. BARKER: Yes. We have good evidence that the pyramidal tracts below the medulla oblongata have been injured in this patient, and the lateral funiculi are doubtless mainly involved. It is possible that there is some involvement of the direct pyramidal tract in the anterior funiculi as well.

Now let us turn to the localization of the lesions causing the sensory disorder. The presence of bathyanesthesia without surface anesthesia in the lower extremities is of great diagnostic importance. One must know a good deal about the anatomy and the physiology of the nervous system, and have clear ideas of the topography of the conduction paths of motor and sensory

impulses in order adequately to localize disturbances of nervous functions such as this patient presents. Professor Sabin has given you a good drill in the anatomic laboratory and Professor Howell has reinforced this in his lectures in the laboratory of physiology. Without such knowledge it would be impossible to work out clues like these. Bathyanesthesia, without surface anesthesia, points to an elective lesion in the sensory conduction path. Now the general sensory conduction path consists of three or four sets of superimposed sensory neurons. First, there is the peripheral sensory neuron, the cell body of which is situated in a spinal ganglion, the long axone-like dendrite, extending to the periphery of the body and the long central axone, entering the spinal cord through the posterior root of a spinal nerve. Once within the cord, this axone gives off collaterals to the gray matter, and then, if it conducts impressions of muscle sense, extends for a longer or shorter distance upward in the posterior funiculus of the cord, first in the funiculus cuneatus of Burdach, and later, in case it is a very long fiber, in the funiculus gracilis of Goll, ultimately terminating in a synapse upon the cell body of a sensory neuron of the second order. The axone of the latter crosses in the sensory decussation of the medulla and passes onward in the medial lemniscus to end in the ventrolateral nuclei of the thalamus. There the path is continued by a sensory neuron of a still higher order to the cerebral cortex (posterior central gyrus).

Now, in the peripheral nerves, the fibers for pain, touch, and temperature sense are intimately mixed with those for deep sensibility (muscle sense; postural sense). It is within the spinal cord that the conduction paths for the several modalities of sensation first pursue more or less isolated courses. The absence of lancinating pains in the lower extremities and of severe spontaneous pain in root zones, as well as the absence of segmental anesthesia and of anesthesia in areas that correspond to peripheral nerve distribution, are all evidence against involvement of either the peripheral nerves or of the posterior roots of the spinal nerves in their extramedullary course. But the presence of ataxia and of bathyanesthesia without surface anesthesia

point strongly to an intramedullary lesion, namely, of the intramedullary continuations of the axones of the peripheral sensory neurons within the posterior funiculi. On the other hand, the paths in the spinal cord for the upward continuation of pain and temperature impulses, namely, Gower's tracts, appear not to be involved, despite the evident lesions of the adjacent pyramidal tracts in the lateral funiculi. Taking all these points into consideration, I think we may be quite sure that we have, in this patient, to do with combined injury and degeneration of parts of the posterior and lateral funiculi of the cord. We have, therefore, fairly satisfactorily localized the lesions. The topographic diagnosis points to these posterior and lateral funiculi of the white matter on both sides; that is to say, we have to deal with combined changes in these four divisions of the white matter of the spinal cord. So much, then, for the localization of the lesions.

The next point to be considered, as far as the time at our command allows, is the nature of these lesions that we have localized. It really requires more than one hour to deal adequately with such an interesting case as this. In the few minutes that remain I shall try to draw some valid conclusions regarding pathogenesis.

First of all, we might be dealing here with taboparesis; that is to say, with a combination of locomotor ataxia with general paresis of the insane, a *parasyphilis*. We know that in 48 per cent. of autopsies on general paretics there are lesions in the posterior and lateral funiculi of the spinal cord. But in this case we can rule out taboparesis. How?

STUDENT: By the absence of the Argyll Robertson pupil.

DR. BARKER: Yes. This fact is strongly against tabes and against general paresis. Another fact against both these conditions is the fact that the cerebrospinal fluid has been tested in this patient and shows no increase in cells in 17 fields examined. Moreover, the Wassermann reaction in the spinal fluid is negative. The report on the blood Wassermann has not yet been handed in. It is true that the gold-sol test on the spinal fluid shows a luetic curve, but in the absence of any increase in the

cell count, and with negative globulin and Wassermann reactions, I think we can safely rule out both tabes and general paresis. You might ask, Could it be an arrested tabes? I think not. Some explanation other than syphilis must be found for the ataxic paraplegia of this patient.

Next, we may consider the possibility of the existence of *multiple sclerosis*. There are multiple lesions in the spinal cord and they are probably sclerotic lesions. There are, however, three points that may be urged against a diagnosis of multiple sclerosis. First, this patient is rather too old for it. Multiple sclerosis is essentially a disease of youth and makes its appearance usually between the fifteenth and the thirtieth year. In the second place, the abdominal reflexes in this patient are little, if at all, affected, whereas in multiple sclerosis they are usually absent. In the third place, symptoms or signs referable to the brain or to the optic nerves are always present in multiple sclerosis, whereas here there are no signs of cerebral involvement. So, for all these reasons and for others which might be adduced were there time, I think that multiple sclerosis may be ruled out.

At this point we may ask ourselves whether we may not be dealing with a transverse myelitis with a partial involvement of the white matter of the cord—in other words, with a *myelitis transversa incompleta*. We know that this disease can yield a clinical picture something like the one we have here. The mode of onset and the mode of progress of the disease are wholly different in transverse myelitis from those recounted by our patient. No myelitic lesion at a single level could account for the phenomena before us. So I think we may rule out *myelitis transversa*.

These several exclusions bring us back to the diagnosis of the only condition that in my opinion accounts for the findings. I may add that this opinion is shared by my colleague who is in charge of the neurologic department of the hospital, Dr. H. M. Thomas, and also by those who have studied the patient in the wards of the hospital. The condition is a form of *funicular myelitis*, sometimes called an *anemic focal intrafunicular leuko-*

myelitis, since there are foci of degeneration and sclerosis in the white matter of the spinal cord, especially in the posterior and lateral funiculi. As a rule, the white matter alone is involved; the gray matter is but slightly, if at all, affected. The disease is commonly associated with anemia and cachexia, and the cord changes were formerly regarded as due to the anemia, but, as I said in the beginning, investigators are coming more and more to the opinion that the lesions of the nervous system and the anemia are due to a common cause. In this case, as in others I have seen and like a number in the literature, the development of the cord changes is more striking than that of the anemia. Combined sclerosis is probably a unitary disease; in it the lateral and posterior funiculi undergo destructive changes; anemia may develop either before or after the symptoms of disease of the spinal cord make their appearance. As Henneberg has remarked, when the anemia is severe and appears early in the disease the patient may die before the changes in the spinal cord are recognized clinically, so that they are discovered first at autopsy. It is usually stated in text-books that anemia and cachexia are the first symptoms, but in our experience there are a number of cases in which the symptoms and signs of changes in the cord appear first and the anemia only later on. The case now before us seems to be a remarkably good illustration of this class. What did the examination of the patient's blood reveal?

STUDENT: Red blood cells, 3,500,000; white blood cells, 8200; Hb., 80 per cent.

DR. BARKER: There is, as you have heard, a high color index. It is 1 plus. How about the differential count of the white corpuscles?

STUDENT: The differential count was: P. M. N., 58 per cent.; P. M. E., 12 per cent.; P. M. B., 0 per cent.; S. M., 24 per cent.; L. M., 4 per cent.; trans., 2 per cent.

DR. BARKER: The platelets are normal in number or but slightly increased. There is only a slight poikilocytosis and no marked anisocystois. There is no leukopenia. The findings are far from being typical, as you see, of an Addison-Biermer anemia.

One point of importance is the existence of oral sepsis in connection with many cases of funicular myelitis. In this instance there is some oral sepsis. There is also no free HCl in the stomach contents; indeed, there is a deficit of 20 acidity per cent. In most cases of pernicious anemia with combined sclerosis there is a benign achylia gastrica.

You have heard that the blood examination reveals the presence of 12 per cent. of eosinophils. This fact makes us think of the possibility of worm invasion. We know that such invasion can produce a pernicious anemia. Invasion of the intestine by the large fish-tapeworm, *dibothriocephalus latus*, is accompanied by a severe anemia. Anemia due to this cause presents, clinically, all the symptoms and findings of a severe hemolytic anemia, but severe anemia in this country is rarely due to it. In Finland and among the Esquimaux *dibothriocephalus anemia* is not uncommon. The explanation of the eosinophils in our patient has not yet been found, though doubtless further observation will provide it.

Taking all the data into consideration, I think there can be no doubt that we are justified in making a diagnosis of funicular myelitis, or of combined sclerosis of the spinal cord, in which the anemic changes are slight and are late in making their appearance, though there must be outspoken changes in the spinal marrow.

Colin Russel, in considering this group of cases, divides the course of the disease into three stages: First, a period of mild ataxic paraplegia, occupying one-half to three-fourths of its whole duration. Second, a period of complete spastic paraplegia, with loss of sensibility in the lower extremities and the lower part of the trunk; this occupies about one-half of the remaining time. Third, a period of flaccid paraplegia covering the rest of the course in which there is elevation of temperature, general malaise, and asthenia, with an increase of the anemia. In the present instance the patient seems to have entered upon the second stage. As time goes on the anemia, asthenia, and general disturbance of metabolism will probably increase, though we shall do all in our power to arrest or to slow the process.

I may mention here that only last week I saw another case of this kind in which the typical tingling of the fingers and toes, the oral sepsis, and the benign achylia gastrica were all present. The patient's red blood-cells, however, numbered 4,000,000, and his hemoglobin was 90 per cent. There was only a little poikilocytosis. I think there can be no doubt of the diagnosis, but it is interesting to have the case come under observation at such an early stage, especially as it will give us opportunity to try and see if it can be arrested at this point by energetic treatment.

Our time is exhausted, but before we close let us ask ourselves What actually causes these lesions in the spinal cord? In answer, we are obliged to say that as yet we do not know. We do know, however, that the injury is in some way related to the blood-vessels that enter the white funiculi of the spinal cord. The first changes that have been observed at autopsy include a few sharply defined areas of sclerosis in the central part of the posterior funiculi in the cervical or lumbosacral regions, or else in the lateral funiculi in the middle cervical or in the thoracic cord. Proliferation of the neurolgia has also been observed with the formation of lacunæ. Somewhat similar changes can be seen in the lateral funiculi in the lumbar regions. The areas of degeneration are small at first, though they gradually enlarge; sometimes there is confluence of smaller foci into a larger area. Some poison evidently arrives through the blood-vessels and starts a degenerative focus, which spreads from its original site so as to make an ever larger focus. Secondary degenerations, of course, follow upon the focal destructive lesions. The involvement of the white matter of the cord is not confined to any specific kind of nerve-fiber. Though it happens that the fibers of the sensory paths in the posterior funiculi and the fibers of the pyramidal tracts in the lateral funiculi are predominantly involved, we are dealing with a pseudosystemic process, not with a true system disease. The lesions transcend the system limits, it being more or less accidental that certain definite conduction paths fall within the destroyed areas. What the noxa is that injures the nervous

system on the one hand and the hemopoietic system on the other we must try hard to ascertain. In investigating this problem it may turn out that the almost constant association with oral sepsis and with benign achylia gastrica is significant. You will note how unsatisfactory our knowledge of the real nature of the disease is as yet.

To the student beginning the study of clinical neurology the symptom-complexes presented by combined sclerosis of the posterior and lateral funiculi may seem particularly puzzling. For in one case the symptoms pointing to the posterior funiculi may predominate, in another those pointing to the lateral funiculi may predominate, and in a third the symptoms may suggest almost equal involvement of the posterior and lateral funiculi. Thus in a patient whose pyramidal tracts have suffered most, the hypertonicity, the hyperreflexia, and the paraparesis will be the striking symptoms, and a little ataxia, a little tingling and numbness in the fingers and toes, and slight bathyanesthesia may be almost the only symptoms pointing to the posterior funiculi. The patient before us with his spastic-ataxic paraplegia, and inability to walk, is a good example of this type. But in a patient whose posterior funiculi have suffered most, the clinical picture may much more closely resemble that of tabes dorsalis (ataxic gait; hypotony; loss of knee-jerks and ankle-jerks; bladder weakness), though a little paraparesis and positive Babinski signs may be present as marks of the injury to the lateral funiculi. The only safe way to proceed, especially for the beginner, is the one I have indicated, that of first painstakingly accumulating the data regarding disturbances of motility, sensibility, and reflexes; second, carefully scrutinizing the data with reference to localizing marks, and, finally, through a consideration of the patient's history and status as a whole, arriving at a conclusion regarding the nature of the disease process and its pathogenesis.

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CLINIC OF DR. JULIUS FRIEDENWALD

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PERSONAL EXPERIENCE IN THE TREATMENT OF ULCER OF THE STOMACH

Brief Review of the Various Medical Methods of Treating Peptic Ulcer; The Leube Cure; the Lenhartz Cure; the Sippy Cure; Comparative Results of the Various Forms of Treatment; Einhorn's Duodenal Alimentation; Brief Discussion of the Surgical Treatment. Advantage of Pyloroplasty Over Gastroenterostomy. Method of Determining When an Ulcer Has Been Healed After Treatment.

SINCE Cruveilhier first advised an exclusive milk diet in the treatment of ulcer of the stomach, and Brinton first pointed out clearly the advantages of the rest treatment in this affection, much interest has been manifested by the medical profession in the treatment of this disease. Inasmuch as the etiology of this affection has not as yet been entirely satisfactorily established, many variations in treatment have been instituted, depending much on the individual views regarding its etiology. Rosenow's recent work has materially altered our views regarding the etiology of ulcer.

According to this investigator the cause of this disease is, in most instances, in all probability a hematogenous infection with special strains of streptococci absorbed from some focus of infection.

On this account the view is now generally maintained that previous to instituting treatment all sources of focal infection should as far as possible be removed. This infection may be dental, tonsillar, sinus, gall-bladder, appendiceal, prostatic, or otherwise.

Aside from removing all focal infections prophylactically, much can be done by means of a carefully selected diet in preventing the onset of ulcer of the stomach. As soon as the first symptoms appear the patient should be placed upon an exclusive milk diet. The temperature of the food should be regulated, so that it be given not too hot or too cold.

Anemia, which so frequently accompanies this disease, must be combated. Hyperchlorhydria, which apparently bears some etiologic relation to this condition, must be overcome. There can be no question that healing is apparently prevented in some instances by the action of the acid gastric juice. This fact has been demonstrated by Sippy in his method of treatment of ulcer, in that by instituting neutralization of this gastric juice by the continued administration of alkalies the healing of peptic ulcers in many instances is established. Notwithstanding the fact that Hardt and Dragstedt have demonstrated that when peptic ulcers were produced by streptococci according to Rosenow's method without the presence of hyperacidity or that delayed healing may be maintained in spite of the absence of the digestive activity of the gastric juice; yet, clinically, hyperchlorhydria is usually observed in ulcer, as can readily be demonstrated by means of the Rehfuss method of fractional analysis.

Again, if one takes the occasion to withdraw the contents of the stomach at the time the pain is at hand, one almost always finds in uncomplicated cases of gastric ulcer an excess of free hydrochloric acid. If no free hydrochloric acid is observed one cannot help but be suspicious of some complication or the presence of some other disease.

Certain advances have been made in the medical treatment of peptic ulcer in the past few years. According to the older plan, the *Leube treatment* was almost constantly followed. This consists of placing the patient at complete rest in bed for fourteen days or more upon liquid diet, mainly on milk. Upon such a diet the patient frequently loses much flesh as well as strength.

On this account Lenhartz cautions against the strict ab-

stinence diet in the treatment of ulcer of the stomach, even in those instances in which there is hemorrhage. He bases his conclusions on the fact that since ulcer of the stomach is most frequently accompanied by superacidity and also by an enfeebled condition, it is best to give protein food early to overcome the acidity as well as to build up the system.

In the *Lenhartz cure* absolute rest in bed for at least four weeks is maintained. An ice-bag is placed on the abdomen and left on more or less continually for two weeks. On the first day, even though there be hematemesis, 200 c.c. of iced milk are given in teaspoonful doses together with two raw ice-cold beaten-up eggs.

The eggs are beaten up with sugar, and they are kept cold by placing the cup containing them in a dish filled with ice. The milk is increased every day 100 grams, and one additional egg added; on the ninth day the patient is given 1 liter of milk and the quantity is not increased; on the sixth day raw scraped beef is added, and the quantity is doubled on the following day; on the seventh and eighth days the patient is given some well-cooked rice and zwieback (softened); and on the tenth day raw ham and butter.

The Sippy Cure.—More recently Sippy has evolved a method of treating peptic ulcer which, according to our observation in a large number of cases, has yielded the most gratifying results.

Inasmuch as it is generally admitted that a peptic ulcer heals if its surface is not continuously exposed to the digestive action of the gastric juice, Sippy's treatment consists in protecting the ulcer from the acid corrosion until it is healed by shielding it from the corrosive effect of gastric secretion. He accomplishes this by maintaining a neutralization of the free hydrochloric acid from early in the morning until late at night, usually from 7 A. M. until 10.30 P. M., or during the entire period when food or gastric secretion is in the stomach.

If an excessive secretion is present at night this is removed by aspiration, until the secretion has disappeared.

The neutralization is effected by frequent feedings and

the administration of alkalies, given freely and at frequent intervals.

Nourishment is given from the very onset of the treatment, preliminary starvation and administration of nutrient enemata, common to other forms of medical treatment, are of little value, according to Sippy. The patient remains in bed for three to four weeks. Three ounces of a mixture of equal parts of milk and cream are given every hour from 7 A. M. to 7 P. M. After two or three days soft eggs and well-cooked cereals are gradually added until in ten days the patient receives 3 ounces of milk and cream mixture every hour, 3 or 4 boiled eggs, and 9 to 12 ounces of a cereal each day. Cream soups of various kinds, vegetable purées, and other soft foods may be substituted now and then as desired. One egg is given at a time, and 3 ounces of a cereal at a single feeding, the cereal being measured after it is prepared. The cereal and eggs are given alternately, and taken at the same time as the 3 ounces of mixture of milk and cream.

The total bulk of each feeding should not be over 6 ounces. After a longer or shorter period, according to the condition of the patient, a large variety of soft and palatable foods may be used, such as jellies, marmalades, custards, creams, etc. The basis of the diet, however, should be milk and cream, eggs, cereals, vegetable purées, and bread and butter. Alkalies are administered from the very beginning of the treatment between the feedings to neutralize the acid secretion; powders consisting of heavy calcined magnesia, 10 grains, with sodium bicarbonate, 10 grains, being alternated with powders of bismuth subcarbonate, 10 grains, and sodium bicarbonate, 10 grains. It is also advisable to give the powders every half-hour after the last night feeding for a number of doses.

The after-management of these patients is important; the hourly feedings and alkaline powders must be continued even after the patient is pursuing his regular occupation. If for any special reason the hourly feedings cannot be maintained the three usual meals should be substituted, and the alkaline powders administered at frequent intervals.

There can be no question but that a large proportion of ulcer

cases recover under medical treatment. According to our observations 72 per cent. by the Leube cure, 66 per cent. by the Lenhartz cure, and 86 per cent. by the Sippy method. When an ulcer patient is treated medically he should be treated thoroughly, and ambulatory treatment is rarely advisable. As we have elsewhere shown, the results of ambulatory treatment is exceedingly unsatisfactory, inasmuch as in but from 40 to 50 per cent. of cases so treated is a cure effected. I believe that many ulcer cases do not recover because treatment is not sufficiently prolonged. A rest cure of but a few weeks is often insufficient. In severe cases the patient should be put to bed for from six to eight and even more weeks.

In those instances in which the ulcer is of a severe type, associated with excessive vomiting, pain, or with hematemesis, food should be withheld by mouth for three to five days, and the patient fed by rectum. A Murphy drip, consisting of normal salt solution and containing glucose, is especially to be recommended.

Of the greatest importance in the treatment of certain cases of ulcer, especially those of a severe type accompanied by excessive vomiting and nausea, is the method devised by Einhorn, known as duodenal alimentation. By means of this method food can be introduced directly into the duodenum. The instrument employed consists of a small capsule perforated and attached to a long rubber tube, at the other end of which a syringe can be applied. The tube is swallowed while drinking water, and the instrument soon passes into the stomach, and within an hour or two into the duodenum. Care should be taken to see that it is in place before the feeding is started. This may be done by gentle traction, which shows a slight resistance if the tube is in the duodenum; by aspiration, which will often bring up golden-yellow duodenal juice without any gastric secretion; or perhaps by giving the patient some liquid to drink by mouth and immediately performing aspiration. If the end of the tube is in the stomach, the fluid can be removed. Any liquid food may be employed, but mixtures of milk, sugar, and raw eggs are the most useful. Care should be taken to see that there are no particles in the food that might clog the tube.

The amount at the beginning should be small, 100 c.c. every two hours, beginning early in the morning and stopping late in the evening. This quantity may be gradually increased up to 300 c.c. If eight feedings are given in twenty-four hours and each feeding consists of 280 c.c. of milk, 1 egg, and 1 tablespoonful of sugar of milk the patient will receive approximately 2280 calories, which is ample for an average individual, and if the patient is at rest in bed it is sufficient to allow a gain in weight.

Einhorn has perfected a special syringe with which it is possible to administer the food without disconnecting the tube. Morgan has suggested a method like that of Murphy for giving salt solution per rectum, permitting the fluid to flow from an irrigating jar, and so arranging the pet-cock that the food is taken slowly, the 300 c.c. of nourishment taking about twenty-five minutes. The food should be administered at body temperature and the heating should be done slowly, for if it becomes too hot it is liable to become thick and lumpy. After heating, it is well to strain the food to be certain to have it free from small particles. If the food is administered too warm or too cold it is apt to cause uncomfortable symptoms, sometimes causing the patient considerable shock; a too rapid administration causes flatulence. After each feeding a syringeful of water at 93° F. should be injected, then the pet-cock closed and the syringe filled with air, which should be injected after the pet-cock has been again opened; the pet-cock should then be closed and the syringe disconnected. The procedure is very important and serves to keep the tube clean and empty. The tube is left *in situ* for about ten days, after which it may be withdrawn.

Of the remedies employed in the treatment of peptic ulcer there is one of unusual importance, as it appears to have an almost specific effect in some instances. The drug is atropin, which by depressing the vagus fibers decreases the secretory and motor functions of the stomach. Through the researches of Eppinger and Hess the theory has been advanced that disturbances of the autonomic nervous system (which includes all of the efferent nerve-fivers outside of the cerebrospinal axis ex-

cepting those supplying the voluntary muscles) lead to increased and decreased tonus or excitability, and that through this system the activity of the glands of internal secretion are regulated and controlled. According to this theory, therefore, a gastric ulcer may have as its underlying basis an increased vagotonus, and atropin by depressing this vagus excitability decreases the possibility of gastric irritation. Clinically it has frequently been noted that healing has been effected in obstinate cases of gastric ulcers when patients were systematically treated with atropin or belladonna.

Scarlet red, too, is a useful adjuvant according to our experience in the treatment of peptic ulcer, and while it cannot by any means replace the usual forms of treatment when administered in conjunction with them, it adds materially to the effectiveness of the cure. It is of great help when administered in the ambulatory cases, the effect being even more favorable than the usual remedies, such as bismuth. Inasmuch as scarlet red in no way interferes with the administration of other remedies, such as the alkalies or atropin, these may be administered when indicated at the same time, and, in fact, the effect of the combination is at times most beneficial.

THE SURGICAL TREATMENT OF PEPTIC ULCER

Simple uncomplicated gastric and duodenal ulcers do not require operation. Operation must only be considered when there are complications or when the ulcer has resisted a thorough medical treatment; especially is operation indicated in those cases accompanied by severe and persistent pain; vomiting or hemorrhage or in pyloric and duodenal ulcers accompanied by stenosis. In ulcers situated at other parts of the stomach operation gives but slight relief unless radical procedures (resection or excision) are undertaken. Operation should be promptly practised in all cases of perforation, and ulcers of the stomach accompanied by tumor formation always demand surgical intervention.

The character of the surgical procedure to be selected is of the greatest importance. This, of course, must vary according

to the situation and extent of the ulcer; thus the good effect of gastro-enterostomy is dependent upon the proximity of the ulcer at the pylorus, the closer to the pylorus, the better is the prognosis. According to Finney and myself the results of pyloroplasty and pylorectomy are far better than gastro-enterostomy. In a comparison of 100 cases of pyloroplasty with a similar number of cases of gastro-enterostomy the following conclusions were drawn by us:

1. The operation of pyloroplasty has its greatest indications in the relief of pyloric stenosis due to chronic ulcers situated at or near the pylorus, and on either side of it or resulting from cicatricial contraction following the healing of such ulcers. It is often a useful procedure in cases of hemorrhage due to gastric ulcer on the lesser curvature or to duodenal ulcers which cannot be controlled medically, and which threaten the life of the patient, as well as in chronic dyspepsias due to ulcers which have not been relieved by medical treatment.

3. The operation has certain advantages over gastro-enterostomy and but few of its disadvantages.

3. Such objections as are urged against the operation—*e. g.*, its inapplicability in the presence of adhesions surrounding the pylorus as well as in the presence of active and bleeding ulcers, and also because of the fact that the new opening is not at the lowest point taking advantage of gravity—are, according to our experience, more fanciful than real, since the operation has frequently been performed under these conditions with most gratifying results.

4. The only contraindications to the operation are inability to mobilize the duodenum when adhesions are too dense and thickening and infiltration about the pylorus due to hypertropic forms of ulcerations. These conditions, however, in our experience occur but rarely.

5. The special advantage of this procedure lies in its affording the opportunity to excise all ulcers in the anterior wall of the stomach or duodenum after direct inspection of the parts affected; also the application of treatment to ulcers situated in the posterior walls. It does not greatly disturb the normal

relation between the stomach and intestines, as one finds after pylorectomy or gastro-enterostomy.

From our experience with pyloroplasty the immediate as well as the final results are most encouraging. While in some instances gastro-enterostomy may be the operation of choice, nevertheless we believe that on account of its comparative unsatisfactory end-results it should as far as possible be limited to the relief of stenosis of the pylorus due to malignant disease, and that usually in nearly all other conditions pyloroplasty and pylorectomy are safer and more satisfactory procedures.

According to our observations there were 90 per cent. of immediately successful recoveries and 86.6 per cent. of satisfactory end-results following pyloroplasty, while there were but 82 per cent. of satisfactory immediate recoveries and 77.2 per cent. of satisfactory end-results following gastro-enterostomy.

I feel that a word must be said regarding the question as to whether an ulcer has really healed aside from the fact as is indicated by the relief of symptoms. Baetjer and I were among the first to call attention to the fact, and other clinicians have since corroborated this finding that the degree of healing can be determined by means of the *x*-ray. In ulcer, when the patient is given a rest-cure treatment, all symptoms gradually disappear, and the patient becomes, comparatively speaking, well. This usually takes place in from four to five weeks. At the end of this time, however, if a second bismuth examination is made, we often find the same characteristic signs as in the first ulcer, though the patient shows no symptoms whatever. In a series of ulcer cases that have been examined, in from three to four weeks after an absence of symptoms we have frequently found but little change in the defect or motility of the stomach.

When these patients are given the ordinary diet these symptoms may recur in a short time. If treatment is continued, however, our experience has demonstrated that as the ulcer continues to heal the motility of the stomach returns to a more normal condition, and by making repeated *x*-ray observations over a long period of time we can observe when the ulcer has

healed, and we are thus enabled to determine the progress of healing. This method has been utilized to great advantage by us in many instances.

I cannot conclude the treatment of ulcer without drawing attention briefly to the after-treatment of this affection.

There can be no question but that relapses are frequently due to indiscretions in diet following the cure when the patient is no longer under the control of his physician. The patient should be placed upon a carefully regulated diet free from acids and indigestible food; intermediate feedings should be prescribed and alkalies be given for some months following the cure. When possible it is my habit to have my patients report for re-examinations at periods of three to four months for a year or more, so as to determine the ultimate result of the treatment. I am presenting a diet list which my patients follow as an after-treatment:

DIET LIST FOLLOWING AN ULCER TREATMENT

In addition to the usual meals intermediate feedings should be taken.

MAY TAKE

Soups:	*Meats (minced):*	*Poultry:*	*Bread:*
Clam	Boiled	Boiled	Stale
Mutton	Broiled	Broiled	Toasted
Barley	Lamb	Roasted	Pulled
Rice	Lamb chops	Chicken	Wheat
Vermicelli	Mutton	Turkey	Zwieback
Cream	Mutton chops	Squab	Crackers
Potato	Brains		
Pea	Sweet-breads		
Celery			
Asparagus			

Fish (minced):	*Eggs:*	*Milk:*	*Butter:*
Boiled	Raw	Whole	Vegetables
Baked	Soft boiled	Skimmed	Asparagus
Broiled	Poached	Whey	Spinach
Blue fish	Omelet	Curd	Cauliflower
Bass	Scrambled	Junket	Squash
Haddock	Shirred	Matzoon	Watercress
Halibut		Kumiss	Potatoes
Trout	*Cereals:*	Kefir	Mashed
Mackerel	Rice	Cream	Baked

Fish (minced):
Oysters
Raw
Steamed
Stewed
Broiled
Clams
Broth
Raw
Steamed

Farinaceous Food:
Cornstarch
Tapioca
Sago
Vermicelli

Cereals:
Cracked wheat
Cornmeal
Barley
Oatmeal
Cream of wheat
Farina
Hominy
Grits
Shredded wheat

Fruits:
Pears
Stewed
Peaches
Stewed
Prunes
Apples
Stewed
Baked

Milk:
Pasteurized
Buttermilk

Ice-cream:
Vanilla

Beverages:
Barley water
Oatmeal water
Rice water
Albumin water
Tea (weak)
Coffee
Cocoa

Mineral Waters:
Vichy
Hawthorne
Lithia
Apollinaris
White Rock
Poland

Butter:
Carrots
Artichoke
Lima beans
Lentils
Peas
String beans

Desserts:
Puddings
Rice
Blanc mange
Cornstarch
Bread
Tapioca
Cup custard

Articles of Diet to be Forbidden

Candies
Salads
Fried foods
Alcoholic stimulants
Sweet potatoes
Strong tea
Strong coffee
Cabbage
Salted fish
Smoked fish
Sardines
Salmon
Preserved fish
Beef
Pork
Veal
Crabs
Rich soups
Liver
Kidneys
Duck
Corn
Goose
Potted meats
Corned meats
Stews
Hashes
Sausage
Twice cooked meats
Celery
Beets
Radishes
Hot cakes
Hot bread
Berries
Bananas
Melons
Oranges
Grape-fruit
Lemons
Preserves
Pastry
Pies
Nuts
Tomatoes

The following diet presents our method of feeding during the Sippy Cure. Either sodium bicarbonate with magnesium-calcined or sodium bicarbonate with bismuth subcarbonate are given alternately every hour on the half-hour from 7.30 A. M. to 10.30 P. M.

Hour. A. M.	*Days. 1st to 5th.*	*Sixth.*	*7th to 8th.*	*9th to 10th.*	*11th to 14th.*
7	Milk and cream	Soft egg Milk and cream	Milk and cream	Cereal Milk and cream	Soft egg Cereal Milk and cream
8	Milk and cream	Milk and cream	Milk and cream Soft egg	Milk and cream	Milk and cream
9	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
10	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
11	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
12	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
P. M.	Milk and cream	Milk and cream	Soft egg Cereal	Cereal Egg	Egg Cocoa
1			Milk and cream	Cocoa	Custard
2	Milk and cream	Milk and cream	Soft egg Milk and cream	Milk and cream	Milk and cream
3	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
4	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
5	Milk and cream	Milk or cocoa Soft egg	Cereal Milk and cream	Milk toast Egg and cocoa	Milk toast Egg and cocoa
6	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
7	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream

Milk and cream each 1½ ounces

Hours. A. M.	*Days.* *15th.*	*16th.*	*17th to 18th.*	*19th.*
7	Egg, cereal Milk and cream	Egg, cereal Milk and cream	Soft egg Cereal Cocoa	Milk and cream
8	Milk and cream	Milk and cream	Milk and cream	Milk and cream
9	Milk and cream	Milk and cream	Milk and cream	Chicken broth
10	Milk and cream	Milk and cream	Milk and cream	Milk and cream
11	Milk and cream	Milk and cream	Milk and cream	Milk and cream
12	Milk and cream	Milk and cream	Milk and cream	Milk and cream
P. M.	2 eggs cocoa	Egg, milk Cream-milk	Minced chicken	Minced chicken
1	Milk toast	Toast Vanila Ice-cream	Milk Milk toast Vanilla Ice-cream	Cocoa Dry toast Vanilla Ice-cream
2	Milk and cream	Milk and cream	Milk and cream	Milk and cream
3	Milk and cream	Milk and cream	Milk and cream	Milk and cream
4	Milk and cream	Milk and cream	Milk and cream	Milk and cream
5	Milk toast Egg, cocoa	Milk toast Egg, cocoa	Milk toast Egg, cocoa	Milk toast Egg, cocoa
6	Milk and cream	Milk and cream	Milk and cream	Milk and cream
7	Milk and cream	Milk and cream	Milk and cream	Milk and cream

Milk and cream 1½ ounces

Hours. A. M.	*Days.* *20th.*	*21st.*	*22d on.*
7	2 eggs Cocoa 1 slice dry toast Butter	2 eggs 1 slice toast Butter	Milk and cream
8	Milk and cream	Milk and cream	Milk and cream
9	Milk and cream Egg	Milk and cream Egg	Cereal Milk and cream Egg
10	Milk and cream	Milk and cream	Milk and cream
11	Broth	Milk and cream	Milk and cream
12	Milk and cream	Milk and cream	Milk and cream

Hours.	*Days.* 20th.	*21st.*	*22d on.*
P. M.	Minced chicken	1 Lamb or mutton	Chop or minced
1	1 slice dry toast	Chop broiled	chicken
	Butter	Dry toast	Dry toast
	Cocoa	Cocoa	Strained vegetable or
	Spinach	Butter	baked potato
		Asparagus or baked	Cocoa
		potato	Butter
2	Milk and cream	Milk and cream	Milk and cream
3	Broth	Milk and cream or	Milk and cream
		milk and egg	
4	Milk and cream	Milk and cream	Milk and cream
5	2 eggs	2 eggs	Stewed fruit or baked
	Cereal	Cereal	apple
	Milk toast	Milk toast	2 eggs
	Cocoa	Cocoa	Cereal
			Milk toast
			Cocoa
6	Milk and cream	Milk and cream	Milk and cream
7	Milk and cream	Milk and cream	Milk and cream

Milk and cream each 1½ ounces

Modified Sippy Diet followed in some cases of peptic ulcer:

MILK AND CREAM, EQUAL PARTS, 1½ OUNCES EVERY HOUR FROM 7 A. M. TO 7 P. M., NINE TO TWELVE DAYS

A. M.	P. M.	*Medicines.*
7.30	1.30.....	Heavy calcined magnesia.....gr. x.
9.30	3.30–5.30.....	Sodium bicarbonate.....gr. x.
11.30	7.30–9.30.....	
A. M.	P. M.	
8.30	12.30– 2.30.....	Bismuth subcarbonate.....gr. x.
10.30	4.30– 6.30.....	Sodium bicarbonate.....gr. xx.
	8.30–10.30.....	

THREE TO FOUR DAYS FOLLOWING

A. M.	P. M.	
7	3.....	Milk and cream.....ää oz. iss.
11	7.....	
A. M.	P. M.	
9	1 and 5.....	Milk and egg or cocoa.
A. M.	P. M.	*Medicines.*
7.30	3.30.....	Heavy calcined magnesia.....gr. x.
11.30	7.30.....	Soda bicarbonate.....gr. x.
9.30	1.30.....	Bismuth subcarbonate.....gr. x.
	5.30.....	Soda bicarbonate.....gr. x.
	9.30.....	

FOUR TO FIVE DAYS FOLLOWING

A. M.	P. M.	
7–11	3–7	Milk and cream.....āā oz. iss.
9	.....	Oat meal, egg and cocoa.
	P. M.	
	1 and 5	Milk toast, egg and cocoa.

A. M.	P. M.	*Medicines.*
7.30	3.30	Heavy calcined magnesia.....gr. x.
11.30	7.30	Sodium bicarbonate.....gr. x.

A. M.	P. M.	
9.30	1.30	Bismuth subcarbonate.....gr. x.
	5.30	Sodium bicarbonate.....gr. x.
	9.30	

TO BE FOLLOWED FOR SEVERAL WEEKS

A. M.	P. M.	
7	3–7	Milk and cream.....āā oz. iss.
11	.....	Milk and egg or cocoa.
9	1–5	Soft diet without acids.

A. M.	P. M.	
7.30	3.30	Heavy calcined magnesia.....gr. x.
11.30	7.30	Sodium bicarbonate.....gr. x.

A. M.	P. M.	
9.30	1.30	Bismuth subcarbonate.....gr. x.
	5.30	Sodium bicarbonate.....gr. x.
	9.30	

As required, additional sodium bicarbonate.....gr. x to xx.

VARIOUS TYPES OF ACHYLIA GASTRICA AS REVEALED BY THE REHFUSS METHOD OF FRACTIONAL ANALYSIS

In the study of the gastric secretion important knowledge has been obtained by means of the Rehfuss method of fractional analysis. According to this method, the gastric function is investigated by examining small amounts of secretion extracted at frequent intervals after a test-meal by means of the Rehfuss tube. This method has so materially altered our views regarding the variations in gastric acidity that it has become necessary to revise the results of our former analyses both in health and disease. One soon learns from this method of investigation that an analysis of the gastric contents at the end of an hour is by no means sufficient to allow us to draw conclusions as to the degree of acidity which may exist in any particular gastric disorder; for whether there be either a hyperchlorhydria or a hypochlorhydria at hand, the gastric secretion may not have risen to its height at the end of an hour, or may have done so before this time, and thus many phases of the hyperacidity or hypo-acidity may be entirely overlooked.

Again, there are many instances of spurious achylias in which at the end of an hour there is an entire absence of free acid, and yet there may be quite an abundance of acid either before or after this period. Many of such cases were noted long before the days of fractional analysis, and were frequently termed cases of gastric hyperesthesia, inasmuch as symptoms of hyperacidity were frequently presented. Relief was afforded in some of these instances by means of alkalies.

Again, there are a number of cases of peptic ulcer presenting an absence of free HCl according to the old method of examination, the cause of which has been difficult to determine. In a certain proportion of such cases we have been able to convince

ourselves that these are spurious achylias and that the acid was present before or after the hour.

In order, therefore, to differentiate between the true and spurious achylias it is necessary to study every case of achylia gastrica by means of a fractional analysis.

In our series of achylias fractional analyses were made in 41 instances. These cases were all true achylias, in which no free hydrochloric acid was secreted during the entire period of digestion; no false or spurious forms have been included in this group.

Of the 41 cases, there were 15 of simple achylia; 4 of chronic gastritis; 3 of gastric ulcer; 7 of carcinoma of the stomach; 3 of pernicious anemia; 2 of cholelithiasis; 2 of pulmonary tuberculosis; 2 of syphilis of the stomach; 2 cases following pylorectomy, and one case following gastro-enterostomy. In addition to these cases there were 37 cases of spurious or false achylias which cannot be properly included in this list. A number of these false achylia cases presented an excess of free HCl at the end of one and three-quarter to one and one-half hours, in several instances of 70 or 75, and were thus really cases of delayed hyperacidity. Rehfuss has called attention to the distinction between psychic achylia in which there is a suppression of the secretion during the first stage of digestion and a chemical achylia; a total absence of both secretions would indicate a complete achylia.

In the simple achylias, in addition to the fact that free HCl is absent in every specimen, the total acidity is observed to be very low, rarely reaching above 10 to 15. In the fasting stomach there is none or but little gastric secretion, and the stomach is empty within two hours, usually between one and one-half and one and three-quarter hours. The ferments are absent or are much diminished. Blood is occasionally found in these cases; sometimes visible, sometimes occult. This is due, as Anderson points out, to the friable state of the gastric mucosa in this disorder, which is very apt to bleed. Bile is frequently regurgitated into the stomach during the early period of digestion, and is often found at the end of twenty to thirty minutes.

In the group of cases of chronic gastritis the same characteristics were observed as one usually finds in simple achylias.

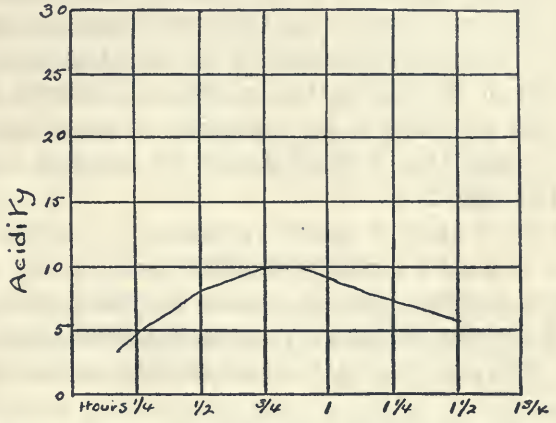

FIG. 283.—Fractional analysis in a case of simple achylia gastrica.

The total acidity is usually higher; sometimes as high as 40 during the period of digestion; in addition, mucus is obtained

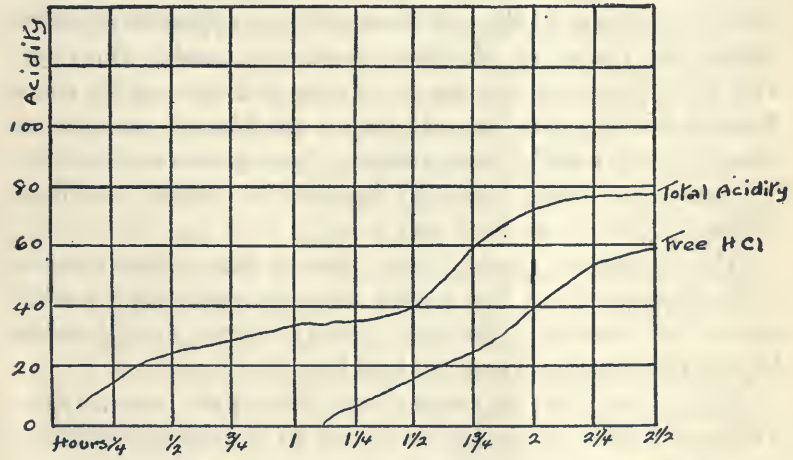

FIG. 284.—Case of delayed gastric digestion or spurious achylia.

in almost every specimen, which is not frequently observed in simple achylia. The motility of the stomach is usually delayed

In 3 of our cases of peptic ulcer there was a true achylia; in none of which was there any free HCl at any time during the entire period of digestion. These cases represent an interesting group which tends to offset the claim of Sippy and others that peptic ulcer is largely dependent for its formation upon the corrosive effect of the acid gastric secretion. However, this condition occurs according to our experience in but so small a proportion of cases that it alone cannot be accepted as definite proof in this regard.

There are 7 cases of gastric carcinoma in our group. The quantities of gastric secretion obtained varies in this condition according to whether there is or is not a pyloric obstruction at hand. In the non-obstructive cases there is a very rapid emptying of the stomach, while in the obstructive forms there is marked retention.

The total acidity varies much in these cases. In 2 the total acidity remained at 10 or below, while in the remaining 5 cases it was much higher in certain specimens: 25 in one, 32 in another, and 43, 52, and 54 in others. In these specimens presenting a high total acidity lactic acid is usually present. Blood is frequently present in the specimens and may appear at any time during the period of digestion; mucus is usually abundant. The Wolff-Junghans reaction is positive and the protein curve diverges quickly from the acid curve; considerable amounts of albumin being usually present within three-quarters of an hour, the quantities being markedly increased to positive reactions within an hour or an hour and a half.

The pernicious anemia cases present the typical features of the true achylias. The fasting stomach contains but a small amount of contents. The total acidity is low, usually below 15, and the stomach is emptied rapidly.

In 2 of our cases of cholelithiasis there were true achylias. The total acidity was as high as 25 and 40 in these cases and the stomach emptied itself rapidly.

In the 2 cases of pulmonary tuberculosis there was a true achylia. The total acidity was low and the stomach was emptied within one and one-quarter hours in both instances.

The 2 cases of gastric syphilis are interesting inasmuch as they presented conditions similar, in respect to the gastric secretion, to those found in carcinoma. The total acidity reached 42 and 56 respectively, the stomach emptying itself rapidly.

In the 2 operated cases (gastro-enterostomies) there was a marked delay in the emptying of the stomach, while in the pylorectomy case there was a hypermotility; in all 3 there was constantly a fairly low total acidity, and the specimens contained bile and mucus.

CONCLUSIONS

1. Fractional analysis of the gastric secretion according to the Rehfuss method is extremely important in all cases of achylia gastrica, inasmuch as by means of this method one can easily differentiate the true achylias from the spurious forms. This differentiation is extremely important, inasmuch as many of the false achylias present a very high HCl acid index; sometimes marked hyperacidity, and are, in fact, really cases of delayed hyperacidity.

2. In the true achylias free HCl is absent in every specimen; the total acidity is low and there is a marked hypermotility.

3. In the form of chronic gastritis associated with achylia there is a high or low total acidity, considerable mucus in almost every specimen, and there is usually delayed motility.

4. In most instances of gastric carcinoma one finds a typical achylia, frequently with delayed motility, and a rather high total acidity and with lactic acid and blood. The Wolff-Junghans test is positive; considerable amounts of albumin being present within three-quarters of an hour, being markedly increased within an hour to an hour and a half.

5. In pernicious anemia one observes the typical features of a true achylia. There is a low acidity and the motility of the stomach is rapid.

CONTRIBUTION BY DR. JOHN RUHRÄH

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SOME OF THE ASPECTS OF EPIDEMIC INFLUENZA IN CHILDREN

THE devastating epidemic of influenza, with which we are all familiar, affected children almost as much as adults, but, fortunately, the cases were, as a rule, light and the mortality low. While this is true, the epidemic presented a large number of rather unusual clinical pictures, to some of which I wish to call your attention today. Among the noticeable features of the disease were certain changes in the eyes. These were usually slight, consisting of a moderate grade of conjunctivitis which lasted from one to three days or more, accompanied generally with a slight degree of photophobia. Occasionally the photophobia was so intense as to suggest meningitis, the child turning away from the light and burying its head in the pillows and objecting bitterly to having its eyes examined in the bright light. Certain other cases, as in the case presented to you, showed a certain amount of edema, especially of the upper eyelids of either one or both eyes, and this was generally attended with a decided pinkish color, which calls to mind the epidemic form of conjunctivitis, commonly known under the name of "pink-eye." Occasionally there was involvement of the ocular conjunctivæ, sometimes only of one eye or only of part of it. All of these eye symptoms subsided promptly, the only treatment being necessary was an antiseptic eye-wash of 1 grain of boric acid and 1 dram of camphor-water and enough distilled water to make 1 ounce. In one or two instances it was noted that the conjunctivitis showed a definite tendency to persist,

but these cases responded promptly to an astringent, such as 1 grain of sulphate of zinc in 1 ounce of distilled water.

The second group of cases shows you three patients with middle-ear affections, one each of the three commonest affections of that organ during the epidemic. In the early part of the epidemic there were but very few ear complications among children, but later on there were quite a number of cases of inflammation. The first child has a marked earache, with a very red throat and only a slight injection of the vessels running along the hammer and a little redness at the upper part of the drum. The second child has a decidedly red drum, but with no evidence of any fluid in the middle ear, but has been suffering a considerable amount of pain. The third child has not only a reddened drum, but bulging, slight deafness with considerable discomfort, and had earache at the onset, but this has very largely disappeared. The first 2 cases will probably be relieved by phenol and glycerin, 25 grains to 1 ounce, instilled at four-hour intervals. The last case should be opened with a free incision.

Not only have there been comparatively few ear complications but also very few involvements of the mastoid, which, if I am correctly informed, is quite different from the epidemic of 1889–90.

You will note that one of these children has a decided hoarseness, with a barking, croupy cough. This patient may serve as a text for a few words on the subject of laryngeal complications in influenza which, while not very frequent, have been exceedingly troublesome. Most of the cases have come on after the attack has been well established, although occasionally the larynx has been involved from the onset. Most of the cases have not been very severe and have not required anything more than the measures usually employed in mild cases of laryngitis. I have, however, seen two instances in which intubation had to be done. One of these children was suffering with nephritis which it had had for many months, and there was some tendency to edema. The onset of the influenza was in the usual manner, but after two days there was a very marked bronchitis and involvement of the larynx producing attacks not unlike catarrhal

spasm, but there was no relaxation in the dyspnea between the spells. The child's voice was not entirely lost, but the dyspnea became so marked that it required an intubation to relieve it. This patient eventually recovered.

The second case occurred in a patient who had influenza complicated with a severe bronchopneumonia. The child became very hoarse, the dyspnea much more marked than the lung involvement would seem to warrant, and gradually the voice was practically lost. There was marked cyanosis and very labored respiration, all of the accessory respiratory muscles being brought into play. The child was intubated and had two days of comparative relief, when the dyspnea again became more or less marked and a very marked toxemia set in, which proved fatal after twenty-four hours' duration. In the second instance the later dyspnea seemed to be due to the extension of the pneumonia and the failing heart.

In addition to these cases, there have been a number of others of a similar nature under the care of other physicians. In these cases of influenzal laryngitis it seems to me to be good practice to have an intubation done as soon as the dyspnea becomes severe enough to bring into play the accessory muscles of respiration, for even if the condition of the child is not very alarming it relieves the heart strain and fatigue incident to forced respiration.

The nose and throat in influenza are worthy of a word. In practically every case there is a more or less marked angina, the inflammation extending over the entire pharynx, tonsils, soft palate, all of these tissues being swollen, reddened, and in some there was a certain amount of pain on swallowing and tenderness on palpating the sides of the neck. In most instances the inflammation extended over the hard palate to the cheeks, but there was nothing that could be called a pathognomonic enanthem. Small punctate hemorrhages were common. The inflammation in the pharynx had a tendency to spread downward, causing a tracheitis and bronchitis, and to spread up through the nose, so that in one or two or three days there was more or less evidence of coryza, but this in children varied a great deal.

In some the nose was dry throughout the entire course of the disease. In other cases there was a rhinitis with a marked purulent discharge from the onset, while in others the discharge did not begin until the second or third day, and consisted chiefly of a more or less clear fluid and had a tendency to excoriate the lip and the skin about the nose. In very young children the rhinitis produced a very considerable amount of discomfort, interfering markedly with nursing and causing mouth breathing.

The nasal condition was treated according to the local conditions, one-half strength Dobell's solution generally being employed for the milder cases, and 10 per cent. argyrol solution for those that were more severe, and where the secretion was thick and tended to dry in the nose, 5 per cent. solution of bicarbonate of soda followed by the use of 5 drops of eucalyptol and 1 ounce of liquid petrolatum afforded considerable relief. In a few instances in order to allow the proper instillation of the various medicaments employed a 1:10,000 solution of adrenalin chlorid was used a few minutes before the treatment. This resulted in shrinking back the mucous membrane so that there was no difficulty in cleansing the nose.

Involvement of the sinuses in children was, in my experience, very rare; certainly nothing beyond what cleared up in the course of the disease without any attention being paid to it.

The odor of the breath was very striking, so that the diagnosis could almost be made on entering the room. This was more marked in some cases than in others, but practically never absent. Where several children were sick in the same room the air became exceedingly disagreeable in spite of good ventilation. The odor is difficult to describe, but not unlike that caused by a decaying human cadaver.

In practically all cases there was sooner or later more or less bronchitis. In a certain proportion of cases, although not a very large one, a pneumonia developed. In young infants this was a bronchopneumonia not differing very much from the types ordinarily seen, except there was probably a greater tendency to cyanosis and extreme prostration. In older children the pneumonia was very often of the bronchial type similar to that

seen in adults, but in some instances it was definitely lobar, at least as far as the clinical picture went. These older cases tended, as a rule, to clear up, but were very frequently complicated by pleural effusions. In some cases the effusion was purulent and a more or less creamy pus of the ordinary empyema being encountered, and these cases were best treated by the usual procedure of drainage. Occasionally a thin pus or what is called "dish-water" pus was encountered, and these cases did very badly without regard to the form of treatment employed, and in a large number of cases the effusion was of a straw color, but contained a considerable amount of pus as shown under the microscope. In these cases the recovery was usually rapid, and the cases which cleared up quickly before it was thought necessary to do a puncture for diagnosis were supposed to have been of this type.

In others the symptoms were very severe, the child being profoundly ill, with a high septic temperature and generally, but not always, a marked leukocytosis. In these cases it often sufficed merely to draw off an ounce or so of fluid for diagnostic purposes and the remainder was rapidly absorbed. In 3 cases there were very severe symptoms which disappeared within forty-eight hours after the puncture and in two of these there was a marked meningismus, so much so that the diagnosis of meningitis had been made on the clinical findings, but all of the nervous symptoms promptly abated with the rapid recovery of the child. In one or two instances where the pneumonia of the lobar type was unduly prolonged and an empyema suspected, the mere puncture by the exploratory needle seemed in some way to stimulate the inflammatory processes, as almost immediate recovery followed even though no fluid could be found.

Taken all in all the outlook in the pneumonic cases in children was very much better than similar cases in grown people. Leaving out the deaths from bronchopneumonia in young infants, the fatalities were comparatively few.

The skin manifestations of influenza are extremely interesting and can be described under several headings. Almost all cases showed a marked flushing of the face. This was a curious

reddish-purple blush over both cheeks, sometimes over the entire face and neck, and there was a certain amount of congestion, sometimes being of a very decided purplish color, at other times the red predominated. This flushing was so constant in children that it can be regarded as a very valuable diagnostic sign. Over the remainder of the body there was more or less congestion, so that the skin paled on pressure; sometimes there was just enough to produce a slight flushing of the skin, at other times, especially in the severer cases, there was a decided stasis of the superficial circulation, and when coupled with heart failure gave the skin an ash-gray-purplish appearance such as is seen in dying persons. Curiously enough, the congestion, while generally of some prognostic importance, was not entirely reliable, as many cases showing marked changes in the skin circulation made a perfectly good recovery.

In addition to the circulatory changes there were several types of skin eruptions seen, none of which could be regarded as pathognomonic. The most significant, which was apparently more often noted in children than in adults, resembled the rose spots seen in typhoid fever. These spots were very variable as regards number and most frequent on the chest, abdomen, and back, and sometimes are noted on the extremities and occasionally even on the face. In one or two instances they were so numerous as to lead to a lay diagnosis of measles. These spots are probably due to invasion of the skin by the influenza virus, whatever that may be, and are similar to the spots in typhoid, to the spots seen in colon bacillus infections, and in certain forms of tuberculosis. There was a very considerable amount of vasomotor disturbance in the skin, so that handling produced spots of redness, and in some cases there were small areas of an urticarial-like eruption.

The gastro-intestinal tract was involved in a great many cases. In a certain number the disease began with vomiting, sometimes there were only one or two vomiting attacks, after which the stomach remained quiet. In others the vomiting was severe and continuous and very much like that seen in recurrent vomiting. Some of these children developed a very marked odor

to the breath, and some of them more or less acidosis, with great prostration and somnolence. In other cases the vomiting was brought on by attempting to feed the child more than he wanted to take. Almost from the beginning of the epidemic it was realized that there was danger of producing vomiting and diarrhea if the child was improperly fed, so that strict directions were left in every instance to give the child plenty of water, small amounts of bicarbonate of soda, either in water or milk, and the only foods allowed were diluted milk, very thoroughly cooked cereals, and a little orange-juice. The food was ordered at three-or four-hour intervals, and instructions left to allow the child to take what it wanted, and then wait until the next feeding time without attempting to force it to take more. Where the child was taking very little food, the amount of fluid given, either in the form of water or diluted orange-juice, was regarded as important, and this was given in small quantities at rather frequent intervals. Where this plan was followed there were very few cases of vomiting or diarrhea apart from those that came on at the onset of the disease. In a few there was a very marked intractable diarrhea with thin watery stools and marked tenesmus. Many of these patients complained of abdominal pain and a certain amount of general abdominal tenderness. These patients usually recovered in a few days.

The temperature charts which I present for your consideration show several different types, all of which were frequently met with. In most of the cases in children under fifteen the temperature was highest at the onset, gradually became lower, and usually reached normal by the end of three days. This led to the term "three-day fever." In others the temperature persisted for five or six days, gradually reaching normal, and occasionally the febrile period was prolonged well into the second week, although most of these cases in which there was a prolonged elevation of the temperature showed some complication to account for it. In other cases the temperature reached normal on the third day, remained down for a day or two, and then recurred for two or three more days, when the normal point was again reached. In almost every instance in which the

child was allowed to be up on the day following the fever and especially if any very marked amount of physical exercise was indulged in there was an immediate return of the fever and other symptoms, and this led to the practice of keeping the children in bed until forty-eight hours free from fever had elapsed, and then allowing them to sit in a chair for half an hour to an hour, gradually increasing the time each day, but carefully guarding against exposure and exercise. In a very large number of cases the temperature became subnormal for two or three days, and the same plan was practised with these cases. In every case where the rule was broken there was a recurrence of fever and of symptoms.

After the first remission of temperature, when the normal point was again reached, any further rise was taken to mean some complicating inflammation, and in all cases where the temperature was unduly prolonged a careful search was made to find an explanation for it, but there were some instances in which this apparently occurred in an uncomplicated form of the disease.

The fatal cases were, for the most part, either due to pulmonary complications, as noted above, or to a very severe general infection. In these latter cases the child was taken suddenly ill, usually with a very high temperature, 105° to 107° F. At the beginning the child was exceedingly irritable and delirious, but soon passed into a more or less comatose condition. There was marked cyanosis of the entire body, and while the heart remained strong, there was a purplish flush of the skin, and as the heart weakened this became the ash-gray color of the moribund. The breathing in these cases was generally not much increased in rate, but at the same time the child seemed to have difficulty in getting the air into and out of the lungs, so that the accessory muscles of respiration were called into play. There was some discharge from the nose, a reddened throat, vomiting if attempts were made to give food or fluid, and generally a diarrhea. The patient sank rapidly, heart stimulants having no effect whatever, and death generally took place within forty-eight hours of the onset. These cases had little to differentiate them from the malignant cases of other infectious diseases unless it was the intense cyanosis.

CLINIC OF DR. GORDON WILSON

MEDICAL DEPARTMENT, UNIVERSITY OF MARYLAND

FUNDAMENTALS IN THE TREATMENT OF PULMONARY TUBERCULOSIS[1]

THE successful treatment of this disease depends almost entirely upon the physician's accurate knowledge of the disease and his patient, and the patient's thorough co-operation and faith in his doctor.

A diagnosis having been established, the doctor must bear in mind that he is treating an *acute exacerbation of a chronic disease*, and that his duty does not end in getting his patients free of symptoms and restored to apparent health, unless he has taught them: (1) that the disease is a chronic one and frequently has long periods when symptoms are absent, (2) that the beginning of an exacerbation is accompanied by symptoms so slight that they may be overlooked, unless watched for, (3) that the "lunger," more than most people, must have a "reserve in health" upon which he can "draw" when needed, and, (4) that the one who remains well is the one who does not believe himself "cured," but knows that he is only "arrested," and lives accordingly.

In breaking the news to your patient that he has tuberculosis, you must remember that to nine out of ten people this means an incurable disease, and no one willingly believes that his case is incurable. Unless you can make your patient *believe* that he has tuberculosis, and that tuberculosis is *curable*, you will have failed in the first essential toward a cure, as ordinarily the patient responds so quickly to a little rest that he begins to doubt that he has anything so "awful as consumption," since he is "getting well so rapidly."

[1] A Lecture to Senior Medical Students.

To the physician, who would start his patient right, the time spent in announcing his diagnosis and giving advice should not be considered unimportant or gone over rapidly, and I believe that more lives have been prolonged or saved by an hour expended at this time, than through an additional month spent later in the "cure." In carrying out this first essential you will, therefore, have to make your patient know and *believe* that he has a "curable" disease, and to do this, it is not enough to state it as a fact, but you must cite examples of persons in his community, known to him, who have had tuberculosis, and who have lived apparently normal lives, or cite such men as Trudeau, who have lived their allotted span and accomplished much. There are very few communities in which there does not live at least one apparently healthy man who "had a hemorrhage when he was young." In driving this fact home don't forget another trait of human nature, namely, that all of us believe more readily "the printed than the spoken word" (as exemplified by the sale of patent medicines by advertisements), and on that account show them in your books that practically no one who has reached the age of fifty fails to show in his lungs, if examined after death, the scars at least of a tubercular infection, no matter what might have been the immediate cause of his death, or whether he had ever been sick in his life prior to his fatal illness. In making your diagnosis known, and in trying to make it be believed, don't hesitate, if necessary to explain to your patient how you arrived at your diagnosis, in other words, why you think he has "Tb." One failing of our profession is the belief that the lay mind is incapable of understanding medical matters, forgetting that we ourselves when medical students had just such minds, but have been made to understand. Not infrequently I have realized that I have not succeeded in making my patient really know that he has tuberculosis, and in such cases I have urged that he see some other *lung specialist*, naming to him a number, so that he will know that I am not referring him to a single man who will "back up" my diagnosis through "medical ethics," a belief by the laity as to "medical ethics" which is somewhat prevalent.

Having accomplished the first essential in making your patient *believe*, the second step follows naturally, and that is for him to make "his confession of faith" and acknowledge to the world that he has tuberculosis by going to a sanatorium, or health resort, that stamps him with the "stigma." Most of the real good, at least of the permanent type, is accomplished after the patient leaves the sanatorium, and is in a great measure due to the fact that he is not ashamed to own up that he has (or has had) tuberculosis, and can live the proper life, while the man who has failed to make "his confession of faith" is always hiding the fact of what has been the matter with him, and, in order to effectually hide it, carefully avoids doing the right things for fear that the world will suspect the truth.

I believe that there should be no exceptions made in telling a person that he has the disease. In one of my cases I refrained from telling the patient what was the matter with her because her family insisted and said that it would kill her, as just a year before, she had lost a favorite niece with laryngeal tuberculosis. After a month's treatment, with very little improvement, I finally persuaded the family to let me tell her, and *explain to her the curability of the disease*, and I have never seen such a marvelous change. She told me that she felt sure from the beginning as to what was the matter with her, and believed her case to be incurable since I was afraid to tell her. Her knowledge as to the course of the disease was limited to the case of her niece, and she dreaded, night and day, the onset of the laryngeal symptoms, which she thought must come, and really feared this horrible torture more than she did death itself. This patient has been an "arrested" case for five years, weighing more now than she ever did, living a normal life, and earning a salary (not "getting one") that many men would envy.

To the second essential, going to a sanatorium or health resort, there are a number of exceptions, and it is at this point that you take up the all-important factor, namely, the treatment of the individual and not the disease. One of the greatest mistakes that we doctors make is to treat a disease, and not the patient who is suffering from it. In no disease that I know of

is it so necessary to modify, or vary, your treatment according to the individual and his symptoms as it is in pulmonary tuberculosis.

You must now consider what your patient is worth, how he earns his living, who are dependent on him, and how he will support himself should he be lucky enough to "arrest" his disease within a reasonable time. Find out from him how long a time he can get from his firm or employer, whether his position will be given back to him when it becomes known that he has tuberculosis, and if the position is likely to be lost, how he can support himself, and those dependent on him, after his disease has become "arrested." To advise a man to go West who has no money, and who has far advanced tuberculosis or active symptoms, generally means not only a marked shortening of his life but also additional physical and mental suffering, to say nothing of the imposition put upon the charity of the community to which he goes. It is most unfortunately true that, other things being equal, the man who has sufficient dollars has a far better chance of a long and useful life than one who has not, and that he who can earn the largest wage with the least expenditure of energy has the best chance.

Some years ago a young schoolteacher consulted me. She was exceptionally well educated in her profession, but absolutely dependent on it. She had an incipient case of pulmonary tuberculosis with distinct but moderate symptoms. To have her sent to Saranac, or Asheville, or Colorado would have prevented her from continuing her life's work, as no school board would have employed her, even though she had no cough and no sputum. To have deprived her of her livelihood in order to check her symptoms would have been malpractice, and in her case I put her under a young doctor in the country who had been a patient and an intern at a well-known sanatorium. After six months' treatment she took up her teaching duties, free of all symptoms, and feeling better than she had ever felt before, and, up to the time I last heard of her, had remained a "clinical cure," and, what is most important, I believe that she was less of a danger to the scholars than any other teacher in that institution.

It is only by a careful study of the individual, not only from the medical standpoint but from every standpoint, that you are justified in allowing a patient with *active* symptoms to remain away from a sanatorium or resort. If the tuberculosis that you find through history, physical examination, or other means is not active, and is, perhaps, of long duration, resort or sanatorium treatment may not be necessary, but you have failed in your duty if you do not convince such a patient that he has a chronic disease, pulmonary tuberculosis, and thus give him the first essential in the cure.

The choice of resort or sanatorium is again an individual requirement, and the only broad rule that I have used is to send my elderly patients to a Southern climate and my younger ones to the climate or section that they prefer.

Another factor that is essential is to make your patient understand that it is not the climate or altitude that will cure him, but *the life he lives in that climate.* I have never sent a patient to Saranac or Asheville, but have sent them to certain doctors in Saranac or Asheville who will treat them, educate them, and control them, so that when they leave the resort they can if they wish continue the cure, but, as Sir William Osler said, the cure of a patient depends much more on what he has in his head rather than what he has in his chest.

The one fundamental truth in treating the active stage of the disease is "rest in proportion to the severity and duration of the symptoms."

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CLINIC OF DR. PAUL W. CLOUGH

From the Medical Clinic of the Johns Hopkins' Hospital

PNEUMOCOCCUS SEPSIS

Sepsis in Contradistinction to Local or Focal Infections. Full Discussion of Symptoms, Prognosis, and Treatment.

The patient whom we shall present to you illustrates some of the features of the most serious sequel of acute lobar pneumonia—a general pneumococcus sepsis.

The patient is a colored man, twenty years of age, who was admitted to the Johns Hopkins Hospital eighteen days ago, complaining of pain in the stomach and side. His past history is unessential save that he has been a heavy smoker, and that in his occupation as driver he has been much exposed to inclement weather. The present illness began twelve days before admission, with pain in the left side of his chest, cough, and loss of appetite. These symptoms gradually increased in intensity, but did not force the patient to go to bed until five days later. In addition to the symptoms already mentioned, he then complained of very severe pain in the side, fever, marked shortness of breath, constipation, and vomiting, which persisted up to his admission.

On admission he looked moderately ill; was mentally clear and alert. The respirations were accelerated, 40 to 60 per minute, with dilatation of the alæ nasi, and a well-marked expiratory grunt. The temperature was 104° F., the pulse 120. There were typical signs of consolidation of the right upper and lower lobes, but not of the middle lobe. The left lung was clear.

The heart was not enlarged. The relative dulness measured 10.5 cm. to the left in the fifth space, and 4 cm. to the right in

the fourth. The first sound was normal in character, and was followed by a soft systolic blow, which was not transmitted to the axilla.

The examination of the blood showed: R. B. C., 6,000,000; W. B. C., 11,500; Hb., 90 per cent. A blood-culture yielded no growth.

The sputum was mucopurulent and streaked with blood. On culture, a pneumococcus belonging to Group IV was isolated.

Urine: Orange; acid; 1022 sp. gr.; trace of albumin; a few hyaline and granular casts. The chlorids were suppressed.

The clinical diagnosis was acute lobar pneumonia due to the pneumococcus; with consolidation of the right upper and lower lobes.

The temperature fell by lysis on the eleventh and twelfth days, reaching normal on one observation. The general condition seemed improved, but no definite change in the physical signs in the chest could be made out. On the thirteenth day, however, the temperature rose to 101° F., and continued to rise, till on the sixteenth day it reached 104.5° F. From this time up to the present there has been a persistent, irregularly remittent fever, ranging from 101° to 106° F., which figure has been reached several times. There has been an increasing tachycardia, roughly proportional to the height of the fever, and also moderate tachypnea.

With the recrudescence of fever the various causes for persistent fever were successively considered. Let us enumerate the more important ones: (1) Empyema. (2) Delayed resolution, including abscess formation. (3) Pneumococcus sepsis. (4) Extension of the pneumonic process to a previously uninvolved lobe. (5) Otitis media. (6) Pericarditis. (7) Pulmonary tuberculosis. (8) Serum disease. (9) Accidental or coincidental infections, not a direct sequel of the pneumonia.

In the discussion of these complications it will be convenient to consider, first, those which could most easily be ruled out, and take up later those which had to be considered most seriously in this patient.

Extension of the consolidation to other portions of the lung could be ruled out by physical examination. Otitis media was sim-

ilarly excluded. No evidence was obtained suggesting the existence of any accidental or intercurrent infection. Pericarditis was watched for, but no pericardial friction-rub was heard, and, in particular, there was no evidence of a developing pericardial effusion. While much less common than empyema, a pericarditis with a purulent effusion is an occasional complication of pneumonia, and a fatal one if it is not recognized and submitted to surgical treatment.

Pulmonary tuberculosis was also considered. Lobar pneumonia may, of course, occur in an individual with active pulmonary tuberculosis, or a latent tuberculous lesion may be aroused to activity by an attack of pneumonia. In either case persistent fever due to the tuberculosis may continue after the high fever of the pneumococcus infection has subsided. In some cases, too, as has been emphasized by Dr. Osler, an acute pneumonia, for a time clinically indistinguishable from a pneumococcus lobar pneumonia, may be caused by the tubercle bacillus, a true acute tuberculous pneumonia; and be recognized only on finding tubercle bacilli in the sputum. In this case repeated examinations of the sputum for tubercle bacilli were made, all with negative results. There was no evidence of tuberculosis in the left lung or elsewhere in the body.

Serum disease did not enter into consideration in this patient, since he received no serum. The only serum therapeutically effective is that active on pneumococci of Type I, and the pneumococcus infecting this patient belonged to one of the other types. Patients with Type I infection who have repeatedly received large doses of serum, quite independently of the occurrence of immediate reactions of an anaphylactic type, not infrequently show late elevations of temperature. These, when they occur, usually come on ten or twelve days after serum is first administered; the temperature frequently reaches 102° to 103° F., and the fever usually persists for about a week, often in association with urticarial eruptions, joint pains, and a moderate degree of prostration. In exceptional cases, however, a more severe type occurs.[1] The fever may persist for two, three,

[1] Bloomfield, A.: The Effects of Serum Therapy in Acute Lobar Pneumonia, Johns Hopkins Hosp. Bull., Baltimore, 1917, xxviii, 301–306.

or even five weeks. It may be high, with irregular remissions. There is usually marked general malaise and prostration, severe aching pains and stiffness of the joints and of the body generally, and often recurring attacks of urticaria. There may be a marked general glandular enlargement, albuminuria and cylindruria, and a high leukocytosis, even as high as 20,000 to 40,000, with (inconstantly) an eosinophilia. Fortunately, such severe reactions are rare, and, as far as reported, complete recovery has always occurred. They may cause serious diagnostic difficulties to those unfamiliar with them.

In this patient empyema was at first regarded as the most probable explanation of his fever, and, as should be done with every patient with pneumonia, the chest was examined daily with special care to detect any signs indicating an accumulation of fluid. No such signs could be made out. There was no significant change in the leukocyte count, which varied from 7500 to 12,000. Had there been anything found on physical examination to suggest fluid, an *x*-ray examination of the chest would have been made, and if doubt still existed, an exploratory puncture over the most suspicious area with a small aspirating needle. An *x*-ray examination should have been made, notwithstanding the absence of suggestive physical signs, since not infrequently the *x*-ray plate may furnish the first definite evidence of fluid, particularly if it is encapsulated between the lobes. Furthermore, in any case where there is a suspicion that an empyema may be developing, it is desirable to have plates taken at frequent intervals for purposes of comparison. These considerations usually outweigh the slight discomfort to the patient involved in such an examination, at least in a well-arranged hospital where the *x*-ray room is in close proximity to the ward.

Delayed resolution of the consolidated lung tissue may be associated with long-continued fever. This may last a few weeks, or even for two or three months, eventually to subside completely, with apparently absolute restoration of the lung tissue to normal. Or in some cases partial organization of the exudate occurs, and a chronic fibroid pneumonia ensues, often associated with multiple small abscesses, which, as a rule, runs a protracted

course, often to end in death. The diagnosis of delayed resolution may be made as an explanation for persistent fever only after all other possible causes for fever have been excluded.

Finally, we had to consider the possibility of an invasion of the blood-stream by the pneumococcus, a generalized pneumococcus sepsis. As a cause of such a recrudescence of fever as occurred in this patient this is fortunately less frequent than is empyema or simple delayed resolution. It is not of rare occurrence, however, and its existence must be suspected in every such case. The diagnosis may sometimes be reached by the demonstration of those secondary or metastatic foci of infection which we know to be most frequent in pneumococcus sepsis; particularly purulent arthritis, acute endocarditis, and purulent meningitis. It is established with certainty by the cultivation of pneumococci in considerable numbers from the blood-stream.

To return to our consideration of this patient, on the eighteenth day of the disease, and the fifth day of the recrudescence of fever, he showed slight jaundice, a symptom which is not infrequent among our colored patients, and which is not necessarily of bad prognostic significance. He was mentally clear and seemed, on the whole, in better general condition than on admission. Respirations were moderately accelerated, but not labored. Signs of consolidation persisted over the right upper lobe and upper part of the lower lobe, but the right base was resolving. The left lung was still clear.

The heart showed no change. The apex was inside the mammillary line, and the sounds normla except for the soft systolic blow noted on admission. The leukocyte count was 7500. A blood-culture was made, from which a day or two later the pneumococcus was isolated. Unfortunately, there is no note in the report of this culture as to the number of colonies developing per cubic centimeter of blood. However, any appearance of organisms in the blood at this stage of the disease, in association with fever of this type which is otherwise unexplained, is strong evidence of the development of sepsis.

Four days later, on the ninth day of the recrudescence, clinical evidence of sepsis was made out. The heart was found

to be dilated. The dulness measured 12 cm. to the left and 5 cm. to the right of the midline. The first sound at the apex was loud and thudding and was followed by an intense systolic blow, well transmitted to the axilla. The pulmonic second sound was definitely accentuated. Along the left sternal border, and maximal in the third left interspace, there was a short diastolic puff. The change in character of the systolic murmur, and especially the appearance under observation of the diastolic murmur, in association with the fever, and the presence of organisms in the circulating blood, indicated definitely the development of an acute pneumococcus endocarditis, involving, in all probability, both the mitral and aortic valves. There was no significant change in the lungs. Blood examination revealed the development of a secondary anemia. The red blood-cells had fallen to 4,000,000 and the hemoglobin to 60 per cent. The development of a secondary anemia is usually a striking feature in all forms of sepsis.

A second blood-culture corroborated the results of the first one and showed the presence of large numbers of pneumococci.

The patient today is in the twenty-sixth day of the disease. His general condition is very much worse. The temperature is elevated (105°F.); the pulse rapid, 120 to 130; respiration 32, moderately accelerated. The leukocyte count has risen to 17,000. The lungs show no change, except that in the left interscapular region there is an area of dulness and enfeebled breath sounds, indicating probably a beginning consolidation on that side. The heart shows the same findings as on the previous examination, although the restlessness of the patient makes auscultation very difficult. A very marked change in the mental state has occurred during the past twenty-four hours. He is now quite irrational and confused. He does not know where he is, and does not recognize those about him. He is restless, and has several times attempted to get out of bed. He does not carry out commands or co-operate at all in the examination. He lies with his head and eyes deviated to the right. The pupils are equal and react to light. There is slight strabismus, the right eye tending to turn outward. Ophthalmoscopic examination

has shown nothing abnormal except slight engorgement of the veins.

His neck is very stiff, and attempts to flex it result in lifting the shoulders of the patient off the bed. There is a coarse tremor of the arms. The limbs are rigid, and any attempt at passive movement meets with resistance. The knee-jerks are exaggerated and there is an ankle-clonus on both sides, more marked on the left than on the right. Plantar stimulation gives an equivocal response. There is a well-marked Kernig sign.

On the basis of these findings a definite diagnosis of meningitis was made, and has been confirmed by lumbar puncture. The spinal fluid was turbid, and microscopically showed large numbers of pus-cells and Gram-positive lance-shaped diplococci.

To summarize: This patient on admission presented the picture of an ordinary acute lobar pneumonia, with consolidation of the right upper and lower lobes. A Group IV pneumococcus was isolated from the sputum. After a transient remission in fever and symptoms on the eleventh and twelfth days, there was a recrudescence of fever, with the development of a general sepsis, as shown by the appearance of large numbers of pneumococci in the circulating blood, and the development of acute endocarditis and purulent meningitis.

By sepsis we understand a more or less generalized invasion of the tissues and fluids of the body by micro-organisms, in contradistinction to local or focal infections, in which the organisms remain localized in a single region. In order that sepsis may develop it is essential that micro-organisms invade the tissues of the body, and give rise somewhere to an infection which at first is more or less definitely localized. The mere accidental penetration of a few organisms into the blood never directly gives rise to sepsis, at least in human infections. The organisms, under conditions unfavorable to the host, may multiply in this primary focus of infection, penetrate from it into the blood- or lymph-stream, and be transported to all parts of the body. The most important mechanism for their dissemination is probably the formation of infected thrombi in the small veins of the inflamed area. From these infected thrombi minute emboli con-

taining bacteria may be continually broken off and carried away in the blood-stream. We then have a septicemia. The organisms which have gained entrance into the blood speedily lodge in the capillaries of the various organs, where, as a rule, they are destroyed without harm resulting. If, however, the organisms happen to lodge in some spot where the local conditions are especially favorable for their growth, they may multiply, and give rise to secondary, or metastatic foci of infection. If multiple abscesses develop in the viscera as a result of such a dissemination of pyogenic cocci, the condition is termed "pyemia."

Whether an infection shall remain localized or whether there shall be an invasion of the blood-stream and a general dissemination of the infection depends on the balance between the virulence, or invasive power of the micro-organisms, and the defensive powers of the host. The mechanism of these reactions is extremely complicated, and differs, in details at least, in case of infections with different species of micro-organisms. Despite the large amount of study devoted to it, our knowledge of the subject is still very meagre, especially as to the part played by the bacteria. In the defensive reaction of the host, simple mechanical factors play a rôle, such as the vascularity of the infected tissue, and the barrier to the spread of infection by continuity which may be interposed by dense connective-tissue capsules, fasciæ, or muscle sheaths. There are also concerned active functions of the tissue cells, and of the phagocytes, and various antibacterial, and possibly antitoxic properties of the blood plasma. The protective properties of the blood-serum are somewhat more thoroughly understood, and in a few instances they may be effectively supplemented by therapeutic administration of immune serum.

By a combination of those factors the body in most instances successfully combats the spread of an infection. Even the entrance of a few organisms into the blood-stream is ordinarily without significance. In the blood the organisms, as a rule, find conditions unfavorable for their growth and multiplication. The blood-stream serves only as a means of transporta-

tion, not as a culture-medium. The continued presence of organisms in the blood means, therefore, a continuous dissemination from some focal infection. If this focus can be removed, the blood speedily becomes sterile. It is only when the organisms are repeatedly entering the blood-stream in relatively large numbers, and over a considerable period of time, that sepsis with its attendant metastatic infections develops.

In occasional cases, indeed, shortly before death there may be such a tremendous increase in the number of organisms in the blood that it seems probable that actual multiplication in the blood-stream has occurred. This, however, is exceptional, and probably indicates a final and complete breakdown of the defensive forces of the body.

The mere presence of a few organisms in the blood occasionally, or even over considerable periods of time, does not constitute sepsis. The latter exists only when organisms are present, usually in considerable numbers, and when their presence is associated with or portends the development of secondary foci of infection. In many infections, essentially localized, a few bacteria occasionally penetrate into the blood, and may be discoverable on culture, without their presence in the blood having any evident significance. To this condition the term "bacteriemia" is given. The distinction is to some extent an arbitrary one, and it may be a difficult one to make in an individual case.

The primary focus of infection is usually at or about the portal of entry of the invading micro-organism. Thus, in the case of a staphylococcus infection of a skin wound, the cut would constitute the portal of entry; the skin and subcutaneous tissues in the immediate vicinity, the primary focus of infection. If, in the ensuing conflict, the invasive powers of the micro-organisms gain the ascendancy, and invasion of the blood-stream occurs, the abscesses in the viscera, in the muscles, in the joints, or in the bone-marrow, which so frequently develop, constitute the secondary or metastatic foci of infection.

The primary focus need not be at the portal of entry of infection, though this is usually the case. Not rarely the invading

micro-organisms cause no lesion at the point of entrance which is noticed by the patient, or which leaves any evidence of its existence. Without denying the possible existence of a minute local infection, the fact is certain that it may be insignificant and transient. Nevertheless, organisms may gain entrance to the blood, may be carried to some tissue in which conditions are favorable for their development, and may give rise there to a local infection which, to all intents and purposes, is primary, and from which a general sepsis with multiple secondary foci of infection may arise. A good example, in the case of Staphylococcus aureus infections, is the (so-called) primary osteomyelitis. While, strictly speaking, a primary osteomyelitis is impossible, the primary superficial infection is only a portal of entry; it is of significance only in opening a pathway for the invading micro-organisms to the susceptible focus in the bone.

With these general principles in mind, let us consider the facts, so far as known, in regard to pneumococcus sepsis, and, in particular, to its most frequent form, that following acute lobar pneumonia. First let us review what is known concerning the presence of the pneumococcus in the circulating blood. It has been known for many years that pneumococci may be present in the circulating blood in pneumonia, but there has been the greatest diversity of opinion as to the frequency and significance of their presence. Some observers found positive blood-cultures in a majority of the cases, from 60 to 90 per cent., or even higher, and attached no special prognostic significance to their presence. Others obtained positive results in only 30 to 40 per cent. of their cases, almost exclusively in patients who died of the pneumonia, and they regarded a positive culture as a sign of very ill omen.

These divergent results as regards the demonstration of the organisms were probably due, in part, to actual differences in the frequency of blood invasion in different epidemics and in different localities; and, in part, to differences in technic. By the withdrawal of relatively large amounts of blood, at least 20 c.c., by making daily cultures from the very onset to the termination of the disease, and by the use of media offering optimum

conditions for growth, a considerable number of positive cultures may be obtained, which would be missed if only a single routine culture were taken.

Jochmann,[1] who at first found organisms in only about 30 to 40 per cent. of his cases, and rarely except in fatal ones, later, by the use of more refined methods of cultivation, and especially by the use of fluid media, obtained positive results in about 75 per cent. of his cases, and regarded a bacteriemia as one of the usual manifestations of the disease.

The difference in the interpretation of the results was also due to the failure at first to recognize the importance of an accurate quantitative determination of the number of organisms present per cubic centimeter of blood.

It is now known that in a large majority of the patients who die of pneumonia, if repeated cultures are taken up to death, positive blood-cultures can be obtained. In general, the number of organisms per cubic centimeter of blood increases as death approaches, and cultures taken shortly before death usually show a considerable number of organisms. Conversely, the majority of patients recover if they have negative cultures throughout their course, or if only a small number of organisms are present, less than 5 per cubic centimeter of blood. The exact frequency of such slight grades of bacteriemia is still unsettled.

While the data I have are insufficient to demonstrate this point, I have the impression that in patients (not serum treated) who recover from pneumonia the earlier in the disease the blood-cultures are obtained, the greater is the probability that a few organisms will be found; and that these tend to diminish or disappear during the latter part of the febrile period, as is the case in typhoid fever. I have also the impression that a reappearance of organisms in any appreciable numbers later in the disease usually marks the onset of an increasing blood invasion, and portends a fatal termination.

The important point to remember, however, is that not in-

[1] Jochmann, G.: Septische Erkankungen, in Handbuch der inneren Medizin., Mohr, L., and Staehelin, R., Bd. I, Infektionskrankheiten, Berlin, 1911, 578.

frequently, perhaps usually, a few organisms may occasionally invade the blood-stream, and that their presence does not unfavorably influence the prognosis. If the number exceeds 5 per cubic centimeter of blood, the outlook is less favorable. If they exceed 15 to 20 per cubic centimeter, the outlook is very grave, unless it be in Type I infections, where some help may be hoped for from serum treatment. If large numbers are present, over 100 per cubic centimeter, the outlook is hopeless; an actual sepsis exists.

In the study of pneumococcus sepsis it is desirable to consider pneumonia as one manifestation of an acute pneumococcus infection rather than as primarily a disease of the lungs. The portal of entry of the infection is undoubtedly the mucous membrane of the respiratory tract. Recent investigations at the Rockefeller Hospital have shown that in a majority of the cases of lobar pneumonia the infection is acquired from an outside source, though it may be caused by a pneumococcus which has been a previously harmless inhabitant of the mouth or throat. The weight of evidence at present seems to indicate that the pneumococcus usually reaches the lung by direct passage downward through the bronchi, though the possibility of its reaching the lung by the blood or lymphatics is not entirely excluded. Here it causes a localized infection which we may regard as the primary focus of infection. From an uncomplicated pneumonic consolidation a blood invasion may arise, and this is doubtless the source in most instances where the invasion occurs at the height of the disease. In cases where sepsis develops after an apparent crisis or lysis, it seems probable that some local complication is to be looked for as the site from which dissemination of organisms has occurred. Those most frequently found are areas of delayed resolution, especially if associated with abscess formation, empyema, or pericarditis.

Pneumococcus sepsis may follow a bronchopneumonia due to the pneumococcus. This has been especially frequent in the secondary bronchopneumonias following measles and epidemic influenza, but it occurs less commonly than in ordinary lobar pneumonia.

Pneumococcus sepsis may also arise from primary foci of infection in the upper respiratory tract. Most important are acute tonsillitis, acute paranasal sinusitis, and especially otitis media, and its sequelæ, acute mastoiditis, sinus thrombosis, and meningitis. Pneumonia occasionally develops as a metastatic infection, in sepsis arising from one of these latter sources.

Other sources of origin of a pneumococcus sepsis are on record, but are of interest chiefly because of their rarity. They need not be considered here.

Why secondary foci of infection develop in some patients with sepsis and not in others is not known. The duration of life after the onset of the blood invasion is certainly an important factor. The longer the patient lives, the more likely it is that such infections will develop. That they may develop with great rapidity, however, is shown by a brief reference to another case history. This patient entered with a lobar pneumonia which terminated by crisis on the fifth day. After two days of continuously normal temperature there was a sudden recrudescence of high fever, and on the second day of this recrudescence clinical signs of aortic and mitral endocarditis appeared.

The clinical symptoms of sepsis depend on the stage of the disease in which the blood invasion occurs, on the rapidity of its course, and on the presence of the various secondary localizations of the infection, and their prominence.

Most often, probably, the blood invasion occurs at the height of the disease, and leads speedily, as a rule, to a fatal termination, without any remission either in the symptoms or the fever. There are often no specific symptoms pointing to the blood invasion, and the diagnosis can be made only by blood-culture. Suspicion may be aroused by rapid deterioration in the patient's general condition, or by evidences of increasing intoxication. There may be some rise in the height of the fever, progressive tachycardia, increasing cyanosis, often tympanites, tremor, delirium, or at times coma, though many patients remain mentally clear throughout the course. Such patients at autopsy often show no evidence of local infection outside the lungs and pleura, and occasionally the pericardium. In other

cases, especially if death does not occur promptly, metastatic areas of infection may develop, though they are often overlooked clinically.

In other patients, such as the case just presented, there may be a remission in both the fever and the subjective symptoms. The respirations become slower, the dyspnea and cough less distressing, the prostration and general discomfort less marked. Sometimes two or three days of completely normal temperature may intervene, though, in our experience, this is unusual. Then there is a rise in temperature for which, at first, there is no obvious explanation, and an increase in the pulse and respiration rate, usually moderate at first; and usually without the pain and dyspnea that prevailed during the primary pneumonia. There is usually headache, prostration, and general malaise proportional to the height of the fever, but for a time these general symptoms may be surprisingly slight, and the mental state quite clear and alert. There is frequently clinical evidence of delayed resolution, and nothing else of significance on physical examination. As a rule, the diagnosis is possible at this stage only by means of a blood-culture. If this method of diagnosis is neglected, the condition will often be overlooked, and can be recognized only by demonstrating the existence of metastatic infections. In the case of pneumococcus sepsis, as already stated, the tissues most frequently involved are the joints, the heart valves, and the meninges.

Acute arthritis is very important clinically, because it is rarely overlooked. It occurred in Musser and Norris'[1] collected statistics in about ½ per cent. of all cases of pneumonia. There is a relatively benign type of arthritis attended by mild local symptoms, with a serous and usually sterile effusion, which generally subsides under symptomatic treatment, and is not associated with sepsis. More frequent and much more important is an acute purulent arthritis. This form is often mono-articular, though it may be polyarticular. It is apt to attack the larger joints, most often the shoulder, or knee, in the cases I

[1] Musser, J. H., and Norris, G. W.: Lobar Pneumonia, in Mod. Med. (Osler), 1907, ii, 537–646.

have seen. The joints are very painful and tender, much swollen, and reddened. On aspiration, purulent fluid containing large numbers of pneumococci is obtained. This form is of the gravest significance because it is usually one manifestation of a general sepsis, which is practically always fatal. Occasionally, however, a purulent arthritis may be independent of a general sepsis, or be the only secondary localization, and under such circumstances recovery is possible. Some permanent damage to the joint usually results unless suitable surgical treatment is employed.

Acute endocarditis is the most frequent and most important of the secondary infections in pneumococcus sepsis. In Musser and Norris' statistics it was recognized clinically in about ½ per cent. of all cases of pneumonia. In their autopsy statistics, however, it was present in over 5 per cent. of the cases. This discrepancy indicates that the diagnosis is made in only about one-half the cases in which endocarditis occurs.

Acute endocarditis is always a part of a general sepsis. Subjective symptoms referable directly to the endocarditis apart from those of sepsis are usually slight or absent. The diagnosis depends on the objective findings of a thorough physical examination of the heart. There is no type of fever that is at all constant or characteristic. The temperature is most frequently high, with irregular remissions, but it may be maintained at a surprisingly constant level. In some cases intermittent fever occurs, and with this type there may be chills and sweats; but aside from a chill at the outset of the sepsis, which is not uncommon, these symptoms are exceptional. Afebrile periods, or periods of slight fever, characteristic of the subacute form of bacterial endocarditis due to Streptococcus viridans, are very rare.

There may be unusually marked tachycardia. There is usually demonstrable a progressive dilatation of the heart, and changes in the character of the sounds, as well as the appearance of murmurs, which indicate the development of valvular defects. Diastolic murmurs, when present, are more significant than systolic murmurs. A soft systolic blow, especially if un-

associated with changes in the first sound at the apex, and best heard over the right ventricle, means very little. If, however, the murmur is intense, if the first sound is sharp, or is muffled or obliterated, if the murmur is well transmitted to the axilla, and the pulmonic second sound is accentuated, the probability of valvular disease is very much greater. On the contrary, there is little room for doubt as to the significance of a diastolic blow, since this is rarely the result merely of muscular relaxation. The development under observation of such endocardial murmurs, in association with the presence of many pneumococci in the circulating blood, makes the diagnosis reasonably certain. Practically all doubt is removed if embolic phenomena occur. These, however, are often absent, especially in those cases which run a rapid course.

The following case history illustrates some of the more common types of embolism in acute pneumococcus endocarditis:

This patient, a colored man twenty years of age, was admitted to the ward on the fifth day of an acute lobar pneumonia. He had had a typical attack of acute rheumatic fever three years before, and had been told that his heart was affected by it. Physical examination on admission showed signs of consolidation of the left upper and lower lobes. The heart was moderately enlarged, the apex impulse in the fifth space, 12 cm. from the midline. There were signs of mitral and aortic insufficiency. Temperature 104° F. Pulse 120. Respiration 48. W. B. C. 18,000. The pneumococcus was cultivated from the sputum. Blood-culture gave no growth. On the ninth and tenth days there was a remission in the fever, which varied from 99° to 101° F., and a corresponding improvement in his general condition. The pulse fell to 70–80, the respirations to 24, the W. B. C. to 8000. The temperature did not reach normal, but during the next week fluctuated between 99° and 101.5° F. Nothing was found on physical examination to explain the fever. In particular, there was no evidence of empyema. The physical signs in the lungs indicated a progressive resolution of the consolidated areas, at about the average rate.

On the eighth day after the remission (eighteenth day of the

disease) the temperature rose to 104° F. Pulse 90. Respiration 24–32. W. B. C. 7400. The patient was alert, complained of headache and of feeling tired; was dyspneic on very slight exertion. The lungs had almost cleared. The heart was more enlarged; the dulness measured 15 cm. to left and 5.5 cm. to the right. The first sound had disappeared; the systolic murmur was more intense, and was now audible in the back. The pulse was more collapsing, and there was an extraordinary degree of throbbing in the peripheral vessels. It was thought that an acute endocarditis had been superimposed on the pre-existing chronic rheumatic endocarditis. A blood-culture revealed the pneumococcus. At that time the importance of determining the number of organisms present was not appreciated.

The patient lived just four weeks, and during this time had a high remittent fever, varying from 100° to 105° F. Embolic phenomena occurred as follows: On the twelfth day of the recrudescence there was pain in the chest, dyspnea, cough, with tenacious sputum mixed with bright red blood, suggesting a pulmonary infarction.

On the thirteenth day he was awakened by severe pain in the region of the spleen, increased by coughing and by deep breathing. There was tenderness on palpation of the spleen and a friction-rub was audible over it. Undoubtedly a splenic infarct had occurred.

At the same time blood appeared in the urine, suggesting also a renal infarct.

On the twenty-first day a second splenic infarct occurred.

On the twenty-third day there was an embolism of the right popliteal artery. He was awakened by severe pain in the leg, worse in the foot and calf, up to the knee, aggravated by moving the leg. He complained also of numbness and a cold feeling in the leg. There was acute tenderness on palpation, the leg was pale and cold, and no pulsation could be felt in the arteries below the knee. Later the circulation became re-established, without gangrene.

On the thirty-second day numerous purpuric spots appeared in the conjunctivæ.

On the thirty-third day there was a cerebral embolism, with left hemiplegia.

Death occurred on the thirty-seventh day. Autopsy report: Acute vegetative and chronic endocarditis of mitral, aortic, and tricuspid valves; infarcts in the myocardium, brain, and spleen; abscesses in the kidneys; acute fibrinous pleurisy; chronic adhesive pericarditis.

While a pre-existing chronic valvular lesion doubtless predisposes to the implantation of an acute pneumococcus infection on the valves, as in this case, it is by no means essential. In many cases previously normal valves are attacked. The mitral valve is most frequently affected, the aortic somewhat less frequently. The valves on the right side are less often involved, but the preponderance of left-sided lesions is somewhat less marked than in rheumatic endocarditis. Anatomically the diseased valves show vegetations which may become very large and polypoid, and ulceration and rupture of the valve frequently occurs. The course is usually acute, the disease lasting from a few days to a few weeks, and the outcome is practically always fatal. It is doubtful if protracted cases, lasting for months, are ever due to the pneumococcus. Such cases reported in the earlier literature were probably due to Streptococcus viridans.

The third important metastatic infection in pneumococcus sepsis is meningitis. As a sequel to pneumonia it rarely occurs except in association with sepsis. In sepsis, either endocarditis or meningitis may occur without the other, but they are associated in about half of the cases in which they occur. It is slightly less frequent than endocarditis, being recognized clinically in 0.4 per cent. of Musser and Norris' series, but was found at autopsy in $3\frac{1}{2}$ per cent. of their cases. Like endocarditis, therefore, it is recognized clinically in only about one-half of the cases in which it occurs.

Its recognition is simple in cases, such as the one presented, where typical symptoms are present. As in this case, the onset of this complication is frequently suggested by a marked change in the mental state. There is often, at first, irritability, restlessness, and delirium, associated with a general hyperesthesia.

Later the condition changes to apathy, stupor, or profound coma, or the condition may be characterised from the start by a gradually increasing stupor. There may be tremor or muscular twitchings, with spasticity of the limbs and exaggerated reflexes. Highly characteristic, when they occur, are paralysis of one or more cranial nerves, most frequently the third or sixth, with a resulting strabismus, marked stiffness of the neck, and a positive Kernig's sign. It is important to remember that these symptoms and signs are often absent, that meningitis will often be unsuspected unless the patient is very carefully watched, and that a definite diagnosis can often be made only by examination of the spinal fluid. The difficulty in diagnosis is further increased by the well-known fact that in pneumonia, as in many acute infectious diseases, the clinical symptoms and signs of meningitis may be present in marked degree, and yet lumbar puncture reveals a normal spinal fluid, and the patient recovers. A state of meningeal irritation, or meningismus, exists, which must be attributed to the local action of some toxin, and is not dependent on the actual presence of organisms in the meninges.

Recently a word of warning has been raised as to a possible danger from indiscriminate lumbar puncture. The work of Austrian,[1] with the meningococcus in rabbits, and of Weed[2] and his associates, with the Friedländer bacillus in cats, and the streptococcus in rabbits, has shown that if a septicemia is produced, such simple procedures as the injection of a small amount of normal serum into the subdural space, or merely the removal of spinal fluid, may precipitate an infection of the meninges by the organisms in the blood-stream.

There is at least a theoretic possibility that a similar infection of the meninges from the blood might be precipitated in patients by lumbar puncture. Indeed, we have seen one case of typhoid fever in which a typhoid meningitis developed three

[1] Austrian, C. R.: Experimental Meningococcus Meningitis, Johns Hopkins Hosp. Bull., Baltimore, 1918, xxix, 183–185.

[2] Weed, L. H., Wegeforth, P., Ayer, J. B., and Felton, L. D.: The Production of Meningitis by Release of Cerebrospinal Fluid During an Experimental Septicemia, Jour. Amer. Med. Assoc., Chicago, 1919, lxxii, 190.

days after an exploratory lumbar puncture, by which a normal fluid, sterile on culture, had been obtained. It would seem safer, therefore, to be conservative in the employment of this procedure, especially if organisms are present in the blood, except in the case of Type I infections, where the demonstration of a meningitis would be an indication for the subdural injection of immune serum.

The outlook in pneumococcus meningitis is extremely bad, though a few authentic cases of spontaneous recovery are on record. It is hopeless if the meningitis is a manifestation of a general sepsis. The study of experimental pneumococcus infection has shown that in the dog,[1] an animal which has a high natural resistance to pneumococcus infection, or in the rabbit,[2] if treated with injections of immune serum, an intravenous injection of pneumococci may be followed by disappearance of the organisms from the circulation, and yet death may occur later from meningitis, although the blood remains sterile. During the brief period of artificially produced septicemia organisms penetrated into the subdural space, where they were able to multiply and give rise to a fatal infection, probably because there they are not exposed to the antibacterial activities of the blood. It seems probable that an analogous condition may occasionally develop in man, and it would be in these cases especially that help might be expected from the intraspinous injection of immune serum in Type I infections. The same would be true in the occasional cases of so-called primary or cryptogenic pneumococcus meningitis which develop independently of pneumonia.

Other localizations of infection in pneumococcus sepsis are less frequent and less important. Among those described may be mentioned otitis media, peritonitis, acute thyroiditis, thrombophlebitis, and muscular abscesses. It is remarkable that the pneumococcus rarely gives rise to some of the lesions so often

[1] Bull, C. G.: Immunity Factors in Pneumococcus Infection in the Dog, Jour. Exper. Med., Baltimore, 1916, xxiv, 7.

[2] Bull, C. G.: The Mechanism of the Curative Action of Antipneumococcus Serum, Jour. Exper. Med., Baltimore, 1915, xxii, 457.

found in sepsis due to the pyogenic cocci, especially to osteomyelitis and to abscesses of the skin, kidneys, and myocardium.

It is frequent to find an acute fibrinous pleurisy, an empyema, or a pericarditis in patients with sepsis. Indeed, an empyema or a pericarditis may be the starting-point of a sepsis, but these lesions frequently and, indeed, usually develop and run their course independently of sepsis.

TREATMENT

The prognosis after sepsis is established is practically hopeless, and all forms of treatment have been futile. Even when no evidence of metastatic infection can be made out, if extensive invasion of the blood-stream has occurred, recovery is excessively rare. We must try by preventive measures to lessen the possibility of the development of sepsis. We need not discuss here the ordinary symptomatic and supportive treatment of pneumonia. The question uppermost in the mind of everyone must be, Have the recent advances in the methods of preparing and standardizing immune serum, and especially in determining the most effective mode of administration made the serum so effective therapeutically that it ought to be used as a routine method of treatment?

The answer to this question must be sought in the published reports of those who have had the largest experience in its use. The favorable reports in Type I infections published by Cole[1] and his associates at the Rockefeller Hospital, supported by those of medical officers from several of the army camps, are convincing, and seem to have established the value of the treatment in these cases. While we are not in a position to make an authoritative statement on the basis of our own limited experience, I feel that we must agree with the recent statement of Nichols[2] that "This method of treatment has passed the experimental stage, and no patient with Type I infection who

[1] Cole, R. I.: Treatment of Lobar Pneumonia, Med. Clinics of North America, 1917, i, 545.

[2] Nichols, H. J.: The Lobar Pneumonia Problem in the Army, New York Med. Jour., etc., 1917, cvi, 219–223.

dies without the early intravenous administration of large doses of Type I serum can be said to have received the best treatment."

If serum treatment is to be beneficial it must be properly carried out. No physician should attempt to administer it until thoroughly familiar with the principles underlying the treatment, with its limitations and possible dangers, and with every detail in its performance. The essential points have been simply and comprehensively discussed in Monograph No. 7 of the Rockefeller Institute,[1] which should be carefully studied by every one who intends to administer serum.

I should like to refer very briefly to a few of the more important considerations. As is now known, pneumococci belonging to different types behave, in their reactions to immune serum, as distinct species of micro-organisms. A Type I serum which is highly effective against Type I organisms has no appreciable activity toward pneumococci of Types II, III, or IV. While immune serum of considerable potency has been prepared for Type II pneumococci, this serum is considerably less effective in protecting animals from infection with Type II organisms than is Type I serum with Type I pneumococci. Furthermore, Cole has concluded that in the treatment of Type II pneumonia in man this serum has little, if any, therapeutic value. The immune serum thus far prepared with Type III organisms has shown such feeble activity in animal experiments that its use in human infections has been deemed unjustifiable. If it were possible to prepare effective immune sera with Type II and Type III pneumococci, a practicable method could probably be devised for immunizing an animal simultaneously to organisms of each of these three types. With such a polyvalent serum, one might feel justified in treating patients with pneumonia without regard to the type of the infecting organism in each individual case, knowing that in 75 to 80 per cent. of the patients, on the average, the infecting organism would be susceptible to the activity of such a serum. However,

[1] Avery, O., Chickering, H. T., Cole, R., and Dochez, A. R.: Acute Lobar Pneumonia, Prevention and Serum Treatment, New York, 1917, Rockefeller Institute for Medical Research.

until an effective serum can be prepared for pneumococci of Types II and III the use of polyvalent serum in infections with these types is futile and deceptive, and as a routine measure, at least, the use of serum should at present be restricted to patients with Type I infection. Fortunately, this type is the one most frequently met with in pneumonia in this country, being found in 30 to 40 per cent. of the cases; and it is one which causes a high mortality if serum treatment is not employed.

For these reasons the determination of the type of pneumococcus concerned in each case should be an indispensable prerequisite to serum treatment, except perhaps in emergencies. The time and labor involved in the type determination is not an adequate excuse for the omission of this procedure. The neglect of this precaution means that one needlessly subjects those patients who are infected with pneumococci of Types II, III, and IV, and who makes up about 60 per cent. of all cases of pneumonia, to the discomfort of the injections and to the possible danger of serum reactions.

If one is dealing with a Type I infection, the treatment should be begun as early in the disease as possible, and should be carried out, as prescribed, by the repeated intravenous injections of large doses of serum until the temperature falls and the general condition is improved. Little can be expected from the use of serum if inadequately administered, or if it is used only as a last resort in patients who have become desperately ill.

If the patient is not seen until an extensive invasion of the blood has occurred, vigorous serum treatment still offers the best chance for recovery if the infection is due to a Type I organism. The outlook is much less favorable, however, than in patients who receive serum early in the disease. That some action is exerted by the serum, even in those patients who die despite serum treatment, is indicated by the fact that the organisms in the blood may diminish in number or disappear after the injections. Even the development of metastatic infections should not cause any relaxation in our efforts. In arthritis or meningitis, removal of fluid and the subdural or intra-articular injection of serum should be carried out.

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THE CLINICAL DIAGNOSIS OF EPIDEMIC INFLUENZA*

INTENSIVE bacteriologic and epidemiologic study of the recent epidemic has failed as yet to establish the etiologic agent. On the clinical side, as well, there exists much uncertainty and confusion as to the identity and diagnosis of the disease. The descriptions of influenza, both as seen in military camps and in civil life, have been meager and inadequate, appearing usually as brief notes preliminary to bacteriologic reports. While nearly all observers agree that the disease begins as a local inflammation in the respiratory tract, there is sharp difference of opinion as to whether the bronchopneumonias are secondary and in the nature of a complication, or whether they are a primary and essential feature. Thus Hewlett,[1] Keegan,[2] Nuzum,[3] Fantus,[4] Soper,[5] and Hall[6] regard pulmonary involvement as a complication or sequel to a primary disease which itself is of uncertain nature. Christian,[7] on the other hand, regards influenza as "a disease involving the respiratory tract"; and Strouse[8] speaks of it as "the epidemic of respiratory disease," since he finds in a large percentage of cases at onset pulmonary signs suggestive of bronchopneumonia. Hirsh[9] refers to the "epidemic of bronchopneumonia"; Friedländer[10] distinguishes types of the disease featured by either coryza, bronchitis, pneumonia, or acute pulmonary edema; Blanton[11] differentiates prepneumonic and pneumonic stages; Synott[12] regards it as primarily an upper respiratory tract infection; and Ely[13] assumes pulmonary involvement from the start. The special committee of the American Public Health Association states in its report[14] that there

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is no known method by which an attack of influenza can be differentiated from an ordinary cold or bronchitis.

A scrutiny of these reports shows that confusion as to the nature of the clinical picture has arisen in two ways: in the first place, by regarding the pneumonias which complicate or follow epidemic influenza as the primary disease, and second, by mistaking for influenza localized respiratory tract infections which are not influenza at all. It seems of the greatest importance to establish, if possible, criteria by which one can distinguish definitely between true cases of epidemic influenza and other diseases. Until this is done etiologic and epidemiologic studies will be greatly hampered. In a previous paper[15] it was pointed out that the disease at the height of the epidemic presented a distinct clinical picture which could be recognized apart from pulmonary complications; a constant set of symptoms, characteristic erythema of skin and mucous membranes, fever of determinate duration, and leukopenia were the main features. It was also noted that as soon as the peak of the epidemic was passed a remarkable change took place in the type of the disease; the symptoms were much less severe, the hyperemic phenomena were much less marked, and the incidence of pneumonia decreased. It is the present purpose to point out that while the disease, as seen since the great wave of the epidemic passed, is less picturesque than the fulminating type, it none the less preserves definite clinical features which make it recognizable and distinguishable from non-influenzal respiratory infections.

Seventy-eight consecutive cases admitted to the Johns Hopkins Hospital during November, December, and January form the basis of this report. Since the clinical picture was systematically described in the previous paper, only those points in which the postepidemic* disease differs from the epidemic form or which are of importance in the differential diagnosis will be considered.

Symptoms.—No essential difference of symptoms was seen

* "Postepidemic" is used in this paper to designate the cases of influenza which have occurred since the sudden wave of the disease in October, 1918.

in the epidemic and postepidemic cases, save that the latter were, as a rule, less severe. Headache, pain in the eyes, general aching, malaise, anorexia, and nausea were the usual complaints. The absence of local symptoms referable to the respiratory tract was even more striking than at the height of the epidemic. If present at all, there was simply slight rawness of the throat, with dry, unproductive cough, stoppage of the nose with a little watery secretion, and conjunctivitis. There was no sharply localized lesion, but the condition was one of diffuse hyperemia of the air-passages, somewhat similar to that seen after the application of a chemical irritant, such as adrenalin. Unless a local complication supervened the hyperemia and its accompanying symptoms usually subsided within two or three days. The tremendous prostration seen during the epidemic did not occur in these cases, and the postinfluenzal asthenia was much less marked.

Hyperemic Phenomena.—As previously pointed out, the severe epidemic cases showed a remarkable dusky erythema which usually persisted into convalescence, and which at times was followed by desquamation. This erythema was in no sense a simple flush, such as is seen in any fever, nor was it dependent on cyanosis; it appeared similar to certain rashes, such as those which occur in scarlet fever, serum disease, or after burns. The distribution, especially over face and neck, the intensity, the persistence after subsidence of fever, and the desquamation were its main features. A striking and characteristic appearance was also noted in the buccal cavity, consisting essentially of an intense hyperemia. Since the height of the epidemic these hyperemic phenomena have been present only to a very slight degree; in most cases there was no obvious change in the skin, although occasionally a slight dusky diffuse erythema was noted. The buccal cavity in the postepidemic cases shows usually only a slight diffuse reddening of the pharynx, pillars, and soft palate, with swelling of the lymphoid tissue on the pharyngeal wall. The appearance is similar to that seen in the epidemic cases, although much less outspoken. From the standpoint of diagnosis the absence of localized inflammatory proc-

esses in the throat seems of importance. There is never any circumscribed tonsillar or pharyngeal exudate or any swelling of regional lymph-glands in uncomplicated cases.

General Physical Examination.—As in the epidemic cases, gross local lesions were strikingly absent, in contrast to the fever and severe constitutional symptoms. In the uncomplicated cases, which made up the majority of the group, examination was negative except for the hyperemic phenomena described above. The lungs were clear and the spleen was not palpable.

Complications.—Bronchitis and bronchopneumonia. It seems of importance to distinguish sharply between the respiratory tract symptoms which are an integral part of the primary disease and those complications in the lung which while frequent and serious are still not an essential feature, although the primary "influenza" may directly predispose to their development. In practically every case at onset there is a diffuse hyperemia of the mucosa of the upper respiratory tract, which gives rise to conjunctivitis, obstruction to nasal breathing, with slight watery secretion, rawness of the throat, and dry tracheal cough, with slight mucoid sputum. These are essential features. Later a series of localized complications is prone to occur, all of which, however, seem to be secondary to the primary disease. Thus, otitis media, paranasal sinusitis, bronchitis, and, finally, bronchopneumonia may supervene. Such complications were, however, relatively infrequent in this series, in contrast to their incidence in large groups of individuals in close contact, as in some military camps, where secondary pneumonia was so frequent as to give rise to the impression that it was an essential feature of the disease. Bronchopneumonia was looked for in our cases with the utmost care, the diagnosis being based on cough, sputum, physical signs, and *x*-ray changes. It was detected in 13, or 16.6 per cent., of the 78 cases. It must, of course, be recognized that the borderline between bronchitis and bronchopneumonia may be uncertain, and that small undetected foci of solidification may exist without being clinically demonstrable.

Other complications were remarkably infrequent. Empyema

occurred in two cases following pneumonia, and in one instance there was an acute sinusitis.

Leukocytes.—In the postepidemic cases, as well as in the epidemic, leukopenia is the rule. The averages of the counts made on various days were as follows:

Day.	Count.
2	6650
3	6100
4	4900
5	6800
6	5100
7	4440
8	4200
9	7150
10	7600
11	7600

The lowest count was one of 1900 on the fourth day. In uncomplicated cases counts above normal were found only in two cases—14,000 (second day) and 13,000 (fifth day).

Leukopenia is, therefore, of great value as a diagnostic point in postepidemic as well as in epidemic cases.

Fever.—The character of individual temperature curves was similar to that of the epidemic cases. As emphasized previously, while the course of the curve shows nothing characteristic, the fever in uncomplicated cases is of strictly limited duration. Table I shows the day of disease on which the temperature became normal in the postepidemic cases compared with the epidemic cases.

TABLE I

Day of disease on which temperature became normal.	—Postepidemic cases.— Number.	Per cent.	Epidemic cases. Per cent.
1			
2	1	1.6	
3	2	3.2	3.9
4	8	13.0	8.5
5	13	21.0	14.2
6	9	14.5	14.0
7	14	22.5	25.0
8	11	18.0	16.0
9	4	6.5	12.5
	62		

Differential Diagnosis.—Despite the confusion which exists, there are but few acute febrile conditions for which influenza can be mistaken. During the period in which this series of cases was seen only 6 patients were admitted to the hospital in whom the diagnosis of influenza made at first turned out to be incorrect. Four of these had acute follicular tonsillitis with localized tonsillar exudate, sore throat, pain on swallowing, cervical adenitis, and leukocytosis of from 12,000 to 15,000. The fifth patient had a local infection of the antrum of Highmore, from which a pure culture of pneumococcus was obtained; the leukocyte count was 13,000. The sixth had an acute otitis media with 32,000 leukocytes. Acute rhinitis and coryza hardly bear a superficial resemblance to influenza. The relative insignificance of the constitutional symptoms, the local lesions, the indefinite duration, and the absence of leukopenia serve readily to differentiate the conditions. It is true, however, that at a time when both influenza and mild respiratory infections are prevalent it may be difficult to tell whether one is associated with or sequent to the other. Differential diagnosis between acute lobar pneumonia and postinfluenzal bronchopneumonia is usually easy. The main points are as follows: In the influenza bronchopneumonias one usually elicits a history of typical symptoms, which may improve after a few days, to be followed later by the more severe symptoms of the pneumonia. These cases showed a striking absence of dyspnea and tachycardia. The tenacious rusty sputum of lobar pneumonia was not seen in any of the postinfluenza bronchopneumonias, but sputum, if present, was fluid and streaked with bright or dark blood. The leukocytes are of special importance, as the leukopenia usually persisted even when pneumonia supervened. This has been the rule in our cases, both mild and severe. The physical signs in the lung are not diagnostic, but sudden onset, rapidly followed by development of signs of lobar consolidation, with tachypnea, pleural pain, rusty sputum, and leukocytosis, speak strongly for acute lobar pneumonia.

The cases which present the greatest diagnostic difficulty are the very mild or abortive ones. There may be simply a

day or two of malaise, anorexia, slight sore throat, headache, or mild catarrhal symptoms. That these cases may really be influenza seems clear from the subsequent development of prostration, with insomnia, tachycardia, or other symptoms.

Diagnosis.—In summary, then, postepidemic influenza still presents a definite clinical picture. As in the epidemic cases, there are striking constitutional symptoms, with at first few or no symptoms referable to the respiratory tract. The physical examination, apart from the hyperemia of skin and mucous membranes, shows nothing definite, in marked contrast to the severity of the symptoms. Leukopenia is the rule during the active stage of the disease. The temperature curves follow the same rules as in the epidemic cases. Except in extremely mild or abortive cases the diagnosis can usually be made with certainty.

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FROM THE GASTRO-INTESTINAL CLINIC OF THE JOHNS HOPKINS HOSPITAL

Notes on the Gastric Signs and Symptoms in Diseases Other than Those of the Stomach

By Thomas R. Brown, M. D.

Gastro-intestinal Disturbances in Metabolic Diseases and Diseases of the Ductless Glands

By John H. King, M. D.

The Rôle of Diet in Treatment of Digestive Diseases

By E. H. Gaither, M. D.

Esophagoscopy

By E. B. Freeman, M. D.

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NOTES ON THE GASTRIC SIGNS AND SYMPTOMS IN DISEASES OTHER THAN THOSE OF THE STOMACH

It is a trite but no less true saying that the greatest danger in modern medicine is the tendency toward intensive specialization. Every specialist, however honest he may be, is singularly prone to find symptoms and signs in most of the cases presented to him that may be regarded as within his own sphere, and to prove to his—and often also to the patient's—satisfaction that by the correction of these symptoms that greatest of desiderata—perfect health—will be obtained. And so ovaries are removed,

kidneys fixed in supposedly normal positions, appendectomies performed, sinuses drained, and tonsils dissected out, displaced uteri suspended and teeth extracted, and yet in many cases—to the patient's grief and the doctor's chagrin—perfect health comes but a step nearer, or sometimes seems even farther away, and the promised goal is still far away—intangible as any ignus fatuus. The reason for this can only be the striking overlapping of symptoms—their singular tendency to be referred to other organs or tissues than those pathologically affected; the ultimate solution of the problem with the optimum result to the patient, the discouraging of a too early entrance into any special field—the ideal, and in fact, the only safe specialist being one who has had early and broad training in general medicine, and, if possible, in general surgery before he commences to confine his activities to a more narrow special field; this is, indeed, the harder, as it is the longer path, but it is the only way out of the wilderness of modern ultraspecialization. There is perhaps no field in which the danger of regarding symptoms of disease as definitely due to pathologic conditions of the organs referred to is greater than in the digestive sphere, and it therefore seemed to us of interest and of real value to discuss briefly and often through illustrative cases of special interest, the gastric signs and symptoms met with in other diseases than those of the stomach itself. The field is so vast, gastric symptoms are so frequently met with as an expression of disease elsewhere, that we can but briefly touch upon many of the points even of special interest. It is needless to call attention to the frequency of gastric symptoms, especially those of hyperchlorhydria, in cases of uncorrected refractive errors, especially astigmatism. Gould has contributed many articles of real interest to this subject, and has attempted to show that many of the great men of the past owed their digestive ill health to such a cause, Huxley, for instance, being a notable example. No less interesting are the nausea and vertigo so frequently found in diseases of the eighth nerve, while, on the other hand, the gastric symptoms met with in tonsillitis, sinusitis, and pyorrhea alveolaris are hardly to be regarded as referred symptoms through vagus or sympathetic

connections, but more as a definite expression of inflammatory changes of the gastric mucosa of toxic or bacterial origin.

Let us briefly discuss the referred gastric signs and symptoms where the stomach itself, both as regards glandular apparatus, mucous membrane, and musculature is absolutely or almost absolutely normal, and where, therefore, signs and symptoms must be regarded as expressions of disturbed innervation of reflex or of toxic nature.

DISEASES OF THE DIGESTIVE APPARATUS ITSELF

Not the least interesting chapter in this story of referred symptoms is that when signs and symptoms are gastric, but the disease is elsewhere in the digestive tract.

In *chronic constipation*, for instance, the major symptoms may be those of an acid dyspepsia, but treatment directed to this condition alone will be singularly unsuccessful, while the gastric picture may clear up as if by magic if the underlying intestinal condition is radically attacked, for, after all, in the vast majority of cases the gastric hyperchlorhydria and achylia are but expressions of extragastric diseased conditions, and to be satisfied with them as diagnoses is quite as pathetic as writing as a case diagnosis headache or jaundice or neuralgia or even endocrinopathy.

If we have a high grade of intestinal stasis due to ptosis, atony, chronic appendicitis, etc., the gastric symptoms may be more stormy—we may have periodic attacks of the most severe symptoms—nausea, vomiting, gastric pain, anorexia, etc., associated with profound prostration, and yet the stomach itself may be an absolutely normal organ. Are the attacks met with in these cases to be regarded as anaphylactic in nature or as a colossal vagotony? Whatever the explanation, the theory of auto-intoxication unquestionably explains best the symptom-complex presented. Is it a toxin normally present but in excess; is it due to the insufficiency of the liver and other portions of the protective mechanism; is there a marked overgrowth of the Gram-positive proteolytic anaërobes; or is there a perversion of ferments or intestinal excretions? It is very striking

what slight changes in molecular constitution are necessary to convert the normal amide bases met with in digestion of the proteins into products of the greatest toxicity, as, for instance, the change from lysin to cadaverin, or arginin to putrescin.

When *true obstruction* occurs the picture is even more interesting. Let us quote then briefly from our notes of a case seen a few months ago, a man whose only complaint was severe epigastric pain, nausea, and vomiting, which he, following alas, the explanation of all patients and many physicians, ascribed to improper diet. A physical examination revealed a very small incarcerated inguinal hernia of the right side with absolutely no local symptoms, and with its immediate surgical treatment the gastric symptoms disappeared as if by magic.

It is superfluous, of course, to call attention to the many cases of *acute appendicitis* in which the only symptoms of the acute inflammation in this organ with its associated local paresis of the nearby gut are purely gastric—epigastric pain and tenderness, nausea, vomiting, and even muscle spasm over the pyloric region—and here, again, a wrong interpretation of the underlying cause and its consequent treatment by purgatives often lead to most deplorable results.

The frequency with which early *intestinal neoplasms* have as their only symptoms a gastric syndrome singularly like that of gastric ulcer with associated hyperchlorhydria is only too well known, and the finding at operation or autopsy of an inoperable carcinoma, often absolutely impossible of diagnosis in its early stages even with most careful *x*-ray and stool studies, comes as a profound shock to the belief in our diagnostic skill. We recall only too well a case of rather vague symptoms in its early stages, but where finally all the symptoms crystallized into the typical picture of pyloric ulcer, which was "confirmed" by *x*-ray studies made by two most capable radiologists, and where because of persistence of symptoms surgery was had recourse to, and an inoperable carcinoma of the sigmoid found, with a normal stomach.

To us one of the most interesting findings has been the gastric picture met with in *cholelithiasis* or even in cases of chronic

cholecystitis and pericholecystitis with adhesion formation. In one case we see the typical picture of a chronic functional dyspepsia—fulness and discomfort after meals, and especially that bane of the gastro-enterologist—gas in incomprehensible amounts, often, of course, but an expression of aërophagy; in the other a picture so like that of gastric cancer with its lack of appetite, loss of weight, etc., that even with the persistent absence of occult blood and the negative roentgenograms, we often are in doubt, and only the operation definitely determines that we are dealing with a case of gall-stones or chronic cholecystitis with no local manifestations.

In both of these types—types especially prevalent among fat women after early middle life—our studies have shown that an achylia, or at least an achlorhydria, is the rule—although, of course, in *acute* gall-stone colic hyperchlorhydria is not at all unusual. In gall-bladder disease these referred gastric symptoms, undoubtedly of vagal origin, are peculiarly interesting in that they have a definite cardiac equivalent—all the signs and symptoms of a cardiopathy being quite often found in this group of cases—symptoms which entirely disappear, with a realization that the heart trouble was functional and not organic, after the appropriate surgical treatment of the gall-bladder. And so we might go on almost indefinitely referring to cases of great interest in duodenum, small and large intestine, and pancreas—singularly interesting examples being the gastric pictures in both acute and chronic pancreatitis, as well as carcinoma at the head of the pancreas—but space does not permit, as we must briefly note the confusing gastric picture so often met with as the main or often the only symptom of diseased conditions in other organs than those of the digestive tract.

DISEASES OF THE PELVIC ORGANS

In our experience the most interesting gastric manifestation of disturbance in this sphere is the occurrence of attacks of periodic and extremely severe nausea and vomiting in cases of marked retroflexion of the uterus, with no local symptoms, and yet with complete disappearance of the gastric symptoms after the sus-

pension of the uterus. We have had 3 such cases within the past year, all previously regarded as cases of pyloric ulcer, and obviously resistant to the usual treatment.

Another interesting picture is that of the acute gastralgias with nausea and vomiting met with in cases of ovarian cysts with twisted pedicles—always extremely difficult to diagnosticate, and frequently regarded as cases of acute appendicitis with only upper abdominal symptoms.

INFECTIOUS DISEASES

We have been singularly interested in the gastric manifestations met with in the acute and chronic infectious diseases, notably *typhoid fever*, *tuberculosis*, and *syphilis*. Certainly the more one studies *pulmonary tuberculosis*, the more one realizes the protean modes of onset met with, and one of the commonest is where the symptoms are truly gastric or gastro-intestinal——a functional atonic dyspepsia in one case, and this is the commonest in our experience, or symptoms of hyperchlorhydria, or nausea with or without vomiting, or, in other cases, intestinal dyspepsia often with diarrhea. It is surprising how many cases come to our clinic complaining only of gastro-intestinal symptoms and without cough or dyspnea, chills, or sweats, where the physical examination shows the gastro-intestinal tract to be fundamentally sound, but the lung definitely involved.

After *typhoid fever* a certain proportion of the cases shows a dyspepsia which careful investigation demonstrates to be associated with an intractable achylia, and in a considerable number of such cases it has taken many months of treatment with acid and appropriate diet before the normal gastric findings are again met with; that they do return to normal, however, furnishes suggestive if not absolutely conclusive evidence that the condition is purely functional.

In *syphilis* we may meet with a protean gastric picture, notably in the tertiary stage, but here the changes are of organic, not functional, nature, but in the parasyphilitic tabes dorsalis we meet with perhaps its most interesting manifestation in the gastric sphere—gastric crises on the one hand, usually re-

garded as attacks of gastric ulcer, or gall-stone colic, or acute appendicitis, and on the other with what we have regarded as its motor equivalent—periodic attacks of intractable vomiting.

In the *arthritides* of infectious origin achylia is the rule, although in our experience acid therapy is not well borne, and often, strange to say, tends to aggravate rather than alleviate the joint symptoms; although we believe Goldthwaite and others still use lactic acid in the shape of buttermilk in large amounts in this group of cases.

DISEASES OF METABOLISM AND OF THE ENDOCRINE GLANDS

The gastric findings in these cases will be discussed at length by Dr. King in this volume, and so we will merely call attention in passing to the frequency with which absence of hydrochloric acid is met with in *chronic gout*, which has led many, notably Von Noorden, to substitute an acid for an alkaline therapy in this disease, and the frequency with which an achylia is met with in both *hyperthyroidism*, Graves' disease, and the reverse condition—*hypothyroidism* or myxedema. Certainly, some of the so-called nervous diarrheas represent early manifestations of an overactive thyroid gland, but why the achylia met with in myxedema is usually associated with an intractable constipation is more difficult to explain.

INTESTINAL PARASITES

It is surprising with what great frequency cases of intestinal parasitism present only gastric symptoms. Here, again, the gastric findings are usually a diminution or complete absence of hydrochloric acid. We well remember a case seen by us a few years ago—a physician from Georgia, about fifty years of age, in whom loss of weight, increasing anemia and cachexia, lack of hydrochloric acid in the gastric contents, and persistent, though faint, traces of occult blood in the stool made one extremely suspicious of gastric cancer. The stool examination made with the greatest care did not, at first, show embryos, parasites, or ova, but one was struck by the enormous number of Charcot-Leyden crystals in the stool, and the blood showing

a marked eosinophilia—over 40 per cent. in this case—made one feel sure that the condition was due to an intestinal parasite. Repeated doses of thymol followed by purgatives finally were rewarded by the finding of ova and embryos of uncinaria—the parasite most loath to leave its intestinal home—and drastic treatment finally led to a complete cure. The case was a singularly illuminating one, and illustrates the importance of thorough microscopic studies of stool and of blood in all doubtful cases.

PERNICIOUS ANEMIA

The association of anemia, nausea and vomiting, and gastric achylia is the classical picture of a pernicious anemia, and every clinician knows the extreme difficulty often met with in differentiating it from gastric cancer. Careful differential blood studies, radiograms—often a frail reed, however—and thorough stool studies with persistent occult blood in the one, absence of occult blood in the other, help in this differentiation, though in some cases only the autopsy findings reveal the diagnosis.

THE PSYCHONEUROSES

Functional disturbances—especially along the course of the vagus—are so common a manifestation of the irritable weakness of the psychasthenic or neurasthenic state that they hardly need be mentioned. Every clinician knows that profound digestive disturbances—anorexia, nausea and vomiting, acid dyspepsia, gastralgia, etc.—may follow sudden or prolonged shock or strain or emotional outbreak and every animal experimenter knows how easy it is to produce a complete temporary cessation of the motor and secretory functions of the stomach by fear, anger, excitement, etc. There are no more interesting group of cases than the so-called psychogenic or neurogenic gastrogenous diarrheas, for example, of which we see many cases every year. Let us quote briefly the history of one such case—a strong, healthy, Irish boy—valet to an irascible master who was subject to violent outbursts of temper. After one such outburst, during which the boy really feared for his life, he developed a diarrhea which still persisted when we saw him several

years later. An achylia was found, and the symptoms rapidly yielded to hydrochloric acid therapy, which, however, could not be discontinued without a reappearance of the diarrhea. In this case there was after a number of months of acid therapy a return of the normal gastric secretions, but this is a rare finding, as in most cases the achylia persists. Obviously, in this case the cause of the achylia was a complete blocking of the vagal path with its stimulating impulses as a result of overpowering fear. Here we have functional derangements in a maximum form, but we must never forget that even every organic lesion is accompanied by some functional disturbance, and the determination of the relative rôles played by organic and functional changes is one of the many fascinating problems that the clinician must solve if he is to expect success.

CARDIOVASCULAR DISEASES

A very wise clinician once said, "When a patient complains of indigestion with no apparent cause, always think of the possibility of beginning myocardial insufficiency; when he or she complains of cardiac symptoms, always realize the probability that these symptoms are of gastric origin." This peculiar overlapping of symptoms in diseases of the heart and of the stomach is, of course, partly due to their close anatomic juxtaposition, partly to their similar nerve supply. Perhaps the most striking example of all is the great frequency with which cases of pure angina pectoris present as their main—sometimes apparently as their only—symptom, the typical picture of an acute indigestion, an error of diagnosis singularly dangerous as evidenced by the number of deaths from so-called "acute indigestion," the vast majority of which are atypical cases of angina pectoris or of cardiac dilatation, a very small minority true cases of acute dilatation of the stomach, and an occasional case representing a true abdominal angina, due in all probability to a claudication or partial cutting off of local blood-supply associated with a sclerosis of certain of the arteries within the abdominal cavity. We remember very well one of these cases in which periodic paroxysms of the most violent epigastric and right hypochondriac

pain with exquisite local tenderness made one think of gall-stone or perforated gastric ulcer or acute pancreatitis, but in which the subsequent course of the case proved beyond peradventure that we were dealing with a case of arteriosclerosis of the mesenteric vessels with attacks of abdominal angina.

Perhaps of equal interest are those cases of just beginning myocardial incompetency in which the only signs and symptoms are those of a mild functional dyspepsia—gas, fulness, feeling of pressure after meals, slight anorexia, etc. In cases where the past history has furnished probable causes for myocardial change, especially in the moderately old and very fat, this possibility should always be taken into consideration, and a short course of very small doses of digitalis may clear up with surprising rapidity symptoms which have proved absolutely refractory to treatment directed to the stomach alone, and rightly so, because the underlying cause was not being attacked—only the symptoms produced thereby. In more marked cases of myocardial decompensation, digestive disturbances are, of course, very common, but here the picture is a simple one, as the symptoms simply represent the disturbances due to the chronic passive congestion and the usually associated gastric achylia, a picture very similar to that met with in parenchymatous nephritis.

DISEASES OF THE KIDNEYS

It is common knowledge how frequently pyelitis and nephrolithiasis are mistaken for gastro-intestinal diseases, notably acute appendicitis and gastric ulcer, and we have already touched upon the functional disturbances of the stomach met with in chronic parenchymatous nephritis. In interstitial nephritis and in tuberculosis of the kidney the picture may be even more interesting. Two cases we especially remember—one in which the progressive anemia and loss of weight, the almost complete anorexia with persistent nausea and periodic vomiting and the gastric achylia had led to a diagnosis of gastric carcinoma, but which a very thorough urinary study showed to be a case of tuberculous nephritis; the other, with almost an identical picture and with the same diagnosis, which urinary studies,

functional tests, and the subsequent history proved to be a case of interstitial nephritis, where eye symptoms, hypertension, and cardiac hypertrophy had not yet made their appearance, and where the only symptoms were those met with in the gastro-intestinal sphere.

We might go on almost indefinitely reciting cases of diseases in various portions of the body where the true nature of the underlying pathologic condition was entirely masked by symptoms referred exclusively, or almost so, to the stomach or intestine. We have shown enough, we feel, to prove the point we made at the beginning of this short article, namely, that there is such an overlapping of symptoms in diseases that the only safe specialist is the one who is not a true specialist, but is the one who, in the more intensive study of special organ or tissue or method, has not forgotten the art and science of general internal medicine, and never overlooks the fact that no organs or tissues can be considered separately, but that each is but a part of the whole, and all are indissolubly linked together by nervous and by vascular connections. Only by a realization of this and by an appreciation of its inevitable consequences can a correct diagnosis be made and rational therapy be instituted.

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GASTRO-INTESTINAL DISTURBANCES IN METABOLIC DISEASES AND DISEASES OF THE DUCTLESS GLANDS

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INTRODUCTION

THE gastro-intestinal tract through the exercise of its manifold activities exerts an important influence upon the normal functions of the body. Disturbances in the normal workings of the stomach and intestines may be primary, resulting from changes originating directly in the gastro-intestinal tract, or secondary, as a consequence of disease processes elsewhere in the body.

There are several primary functions of the gastro-intestinal tract which have an influence on disease processes located in other organs of the body.

I. **The Secretory Function.**—(*a*) The increased secretion of

hydrochloric acid is apt to be associated with pyloric spasm and, later on, gastric atony. Furthermore, hyperacidity frequently interferes with proper ingestion of food, because it may cause painful sensations and even vomiting during digestion.

(*b*) Diminution in the secretion of hydrochloric acid results in the food reaching the intestines in an insufficiently prepared state and also allows a decomposition process to be set up in the stomach, with the resulting clinical symptoms of flatulence, epigastric pressure, and belching of gas. When the condition goes on to complete absence of free hydrochloric acid, the emptying time of the stomach is greatly accelerated, giving rise often to a feeling of emptiness shortly after eating, and epigastric unrest.

II. **The Motor Function.**—Increase in the motility of the stomach and intestines may be associated with an obstinate and very profuse diarrhea, which, occurring in association with some disease in another part of the body, may affect the prognosis very critically.

Decreased motility of the gastro-intestinal tract, particularly in extreme grades, sufficient to produce stagnation, can give rise to vomiting, which may lead to a considerable degree of exhaustion and malnutrition.

III. Decomposition, in the stomach and intestines, is prone to upset gastric and intestinal digestion. Decomposition of the gastric contents is often associated with feelings of giddiness, languor, and headache, a condition called by Trousseau gastric vertigo. Distention of the stomach and intestines may give rise to cardiac distress amounting to actual cardiac dyspnea. With extreme dilation of the stomach, associated with severe grades of decomposition of the stomach contents, the clinical condition called gastric tetany by Kussmaul may occur.

IV. Inflammation of the stomach and intestines, particularly those of an acute nature, have a very unfavorable influence upon disease processes. The occurrence of an acute enteritis, in the course of any critical disease, is always looked upon with grave forebodings.

Disease processes elsewhere in the body often have a marked

secondary effect upon the gastro-intestinal tract. The derangements of the stomach and intestines, though a late development in the clinical picture, may quickly become the dominating features.

The symptoms and signs of a disease entity may be so clear and striking that the diagnosis is at once apparent and certain. The clinician's attention is perhaps then focused exclusively on the main disease process, and important secondary symptoms, which indicate the progress of the disease, are neglected. Furthermore, symptoms which have apparently little significance in themselves are often the means of directing the observer's attention to a serious ailment of the body. Perhaps no domain of the body has more influence over the progress of disease, or conversely, is more influenced by morbid process of the body, than the gastro-intestinal tract. It is therefore important to analyze carefully the signs of derangement of the stomach and intestines, seeking to find out if they point to some more obscure disease, as well as to appreciate their prognostic significance upon a disease process already well established.

The gastro-intestinal tract is the great means of bringing sustenance to the body, and eliminating useless and harmful products from the body. Its normal activity is essential for the good health of the individual, and consequently it plays an important rôle in practically every disease. As long as it functions normally and supplies nutriment to the body, it helps to combat disease. When its functions break down, then disease ravishes the body more rapidly.

It is the purpose of this clinic to call attention to some of the gastro-intestinal symptoms and signs in the diseases of metabolism and the endocrinopathies.

GENERAL METABOLIC DISEASES

Diabetes.—In this disease, where the problem is largely that of maintaining the patient in good nutrition upon a selected diet, special attention must be paid to any derangement of the gastro-intestinal tract.

Gastric Symptoms.—Polyuria and polydypsia do not neces-

sarily predispose to affections of the stomach, especially in the early stages of diabetes. The stomach may function normally in spite of the tremendous amounts of food and liquids that it is called upon to handle. The gastric acidity shows no peculiarity in its behavior, the variations are within the normal limits.

In the later stages of diabetes, when the patient is debilitated and coma is threatening, gastric motility is often very much diminished, with resulting atony and stagnation, loss of appetite, fermentation, and vomiting. A tendency to hyperchlorhydria, associated with burning sensations in the epigastrium, hyperesthesia, and feeling of pressure in the region of the stomach is often associated with the later stages of this disease.

Intestinal Symptoms.—A predisposition to constipation is the rule in diabetes, while diarrhea is much less common. Constipation comes on very easily in this disease, when the carbohydrates, especially bread, are removed from the dietary.

Diarrhea is apt to supervene on a vegetable and fat diet. It is not always an evidence of catarrh of the bowel, as it often comes on in a bizarre form, with a sudden onset and equally sudden cessation, like a nervous diarrhea. On the other hand, diarrhea may result from a true catarrh of the bowel and is a serious symptom, both because it interferes with proper nourishment and often ushers in coma.

When the diarrhea in diabetes mellitus results from a true enteritis the movements are semisolid, often contain considerable mucus, and continue for a long while. When the diet is responsible for the increased evacuations there is associated distention, abdominal cramps, with watery evacuations, followed by almost immediate relief. If disturbances in the external secretion of the pancreas are responsible for the diarrhea, the bowel movements contain an excess of fats and are strikingly offensive.

In general, the resorption of food from the intestinal tract is good, and there is no increase in fats or carbohydrates in the feces. When the external functions of the pancreas are involved as well, then there may be large amounts of undigested fats and proteins in the feces. Stagnation in the bowels with

decomposition exerts a deleterious effect upon the cause of diabetes, and to it is ascribed by some the onset of coma diabeticum.

Coma Diabeticum.—This most fatal complication of diabetes is often associated with striking gastro-intestinal symptoms. It may be ushered in by an acute attack of nausea and vomiting, followed rapidly by onset of coma, or an acute attack of true catarrhal enterocolitis with marked diarrhea may precede the coma. Both of these complications are serious, since they make very difficult the maintenance of the patient's nutrition during the period of coma.

On the other hand, a period of marked constipation may be a forerunner of coma. Here nutrition is not interfered with so seriously, but to the deleterious effects of retained decomposition products and their absorption is ascribed the onset of coma. Diarrhea is in no sense a necessary accompaniment of coma. It is lacking in at least one-half of these cases. On the other hand, long periods of constipation in diabetes must be viewed with care, as they undoubtedly predispose to coma.

Though there are no specific gastro-intestinal disturbances associated with diabetes, any serious derangement of the functions of this tract may influence the course of this disease very deleteriously. It is therefore important to recognize early signs of stagnation or inflammation of the gut, particularly for the purpose of discerning the onset of coma and taking precautions to ward off this most fatal complication. These conditions, though even of a mild degree, must be considered serious and relieved as promptly as possible, since their persistence is a constant danger to the patient.

Gout.—The gastro-intestinal symptoms of gout may be very insignificant, the disease running a long course without anything more than slight constipation and flatulence. However, in other cases, a tendency to severe and uncontrollable diarrhea exists, which may be associated with nausea and anorexia. These symptoms are often the precursors of the gouty paroxysms.

A deficiency of hydrochloric acid secretion may occur in

gout, but it is not characteristic. Such a condition is generally due to a complicating gastritis or general inanition. In the later stages of gout achylia gastrica may supervene.

There is often a definite tendency to intestinal putrefaction in gout, with a high elimination of nitrogen in the feces, without a high percentage of fat in the stools, indicating an increased excretion of nitrogen rather than a diminished absorption.

In retrocedent or suppressed gout, a term which is applied to serious internal symptoms coincident with a rapid disappearance or improvement of the local signs, very severe gastro-intestinal symptoms may develop, consisting of pain, vomiting, diarrhea, and great depression. Such an attack may result fatally.

Obesity, resulting from overindulgence in food or alcohol, is particularly prone to be complicated by disturbances of the stomach and intestines.

The continued strain upon the tone of the stomach caused by overloading with food and liquids results in the end in gastric atony, with its attendant train of symptoms—flatulence, epigastric pressure, and early feeling of satiety.

Many cases of obesity develop a severe type of diarrhea associated with cramps in the lower part of the abdomen, followed by two or three watery movements and expulsions of considerable offensive gas. The bowel movements may contain much mucus and be as frequent as five to ten movements daily.

Another type of severe diarrhea may develop from constipation, resulting from the accumulation of feces, forming hard scybalous masses, which excite frequent movements, or form stercoral ulcers which reflexly stimulate the movements of the bowel.

The most severe and intractable diarrhea is that induced by fatty degeneration of the liver, which may accompany severe grades of obesity.

In the anemic form of obesity, which occurs mostly in women, and is associated with anemia often of the chlorotic type, gastro-intestinal symptoms may be prominent. The appetite is generally poor and, peculiarly, carbohydrates are preferred to proteins by the patient. The tongue is furred and the breath often

foul. Intestinal flatulence associated with constipation is common. Diarrhea is less frequent, but may be severe, due to an acute or chronic catarrhal inflammation of the bowel.

DISEASES OF THE DUCTLESS GLANDS

The Endocrine Glands.—The gastro-intestinal tract shares, with the rest of the organs of the body, in the secondary effects resulting from disturbances in the functions of the ductless glands. Some of the endocrine glands have a very considerable influence on the gastro-intestinal tract both through their effect upon its secretory functions as well as by influence on the autonomic and vegetative nerve-fibers of these organs. Conversely, derangements of the gastro-intestinal tract react upon the ductless glands, particularly when the latter are functioning abnormally. An attempt will, therefore, be made to call attention to some of the more important clinical disturbances of the gastro-intestinal tract, associated with derangements of the ductless glands.

Diseases of the Thyroid.—Disturbances in the normal functioning of the thyroid gland are often strikingly associated with gastro-intestinal symptoms. In fact, the latter may be so pronounced as to completely obscure the fundamental disturbances in the thyroid.

The thyroid gland possesses the properties of stimulating secretion, motility, and accelerating the body metabolism. All these factors have an influence upon the gastro-intestinal tract. When the thyroid is stimulated to overactivity the reaction on the gastro-intestinal tract is striking. Conversely, when the gland is sluggish, a reaction in many ways diametrically opposite is produced on this tract.

Exophthalmic Goiter.—In this disease, associated with hyperactivity of the thyroid gland, the stomach is apparently less influenced than the intestines. However, there may be a complete cessation in the secretion of hydrochloric acid, resulting in practically an achylia gastrica, and the motility of the stomach may be greatly increased. These changes result often in an empty feeling in the stomach after eating, and again, in a striking diarrhea.

Diarrhea may be one of the most frequent and annoying symptoms of this disease. "It may usher in the disease, appear at any time, be transitory, periodic, or remain permanently, and greatly increase the severity of the disease. The stools may even escape involuntarily."

"On the other hand, the diarrhea may be of sudden onset, and appear at the crises of the disease when the tachycardia, ocular, and other manifestations are most pronounced. This may occur both in the early and late stages of the disease."

The movements are fluid, bile-tinged, and often contain whole food fragments a few hours after same have been eaten, indicating an increased peristalsis of the stomach and intestines, in addition to impaired digestion.

This frequent diarrhea may be so prominent and the thyroid signs so obscure that only very careful physical study and pharmacodynamic tests enable the clinician to demonstrate that the diarrhea is dependent on hyperactivity of the thyroid.

Again, the diarrhea takes the type known as the nocturnal diarrhea, characterized by a number of passages of the bowel rapidly following one another in the early morning. These patients often have a ravenous appetite, eat much more than they can digest, and later develop true enterocolitis with mucus in the stools.

In very acute types of Basedow's disease nausea and incessant vomiting may complicate the diarrhea. Many of the so-called nervous diarrheas are secondary to an overfunctioning of the thyroid gland. The diarrhea of exophthalmic goiter has been referred to irritation of the vagus nerve by Eppinger and Hess and by others to the fact that an absence of free hydrochloric acid in the stomach allows the pylorus to remain open, and the food passes rapidly into the intestines in an improperly prepared condition. There results an excessive stimulation of the intestines with a rapid emptying, culminating in frequent watery movements containing undigested food particles. A fatty diarrhea with lowered carbohydrate tolerence has been described. This has been explained by some author on the basis of inhibition of the pancreas by the hyperactive thyroid.

The beneficial therapeutic results from acid medication and dietary are often striking in the diarrhea occurring in hyperthyroidism.

Myxedema.—Diarrhea is extremely uncommon in this disease, in fact, a rather obstinate constipation generally exists. This diametrically opposed reaction of the gastro-intestinal tract seems to indicate a specific action of the thyroid gland in these cases. This is further substantiated by the fact that the diarrhea generally clears up with the reduction in the gland surgically.

Diseases of the Pancreas.—Disturbances in the normal activity of the pancreas may be associated with pronounced gastro-intestinal symptoms. The most striking clinical picture is that occurring in conjunction with acute hemorrhagic pancreatitis. There is sudden violent colicky pain localized in the upper part of the abdomen. Then follows nausea and vomiting, with eventually collapse. The abdomen becomes swollen and tense. Usually there is constipation. Collapse may come on and the patient die as early as the second to fourth day of the disease.

Impairment in the external secretion of the pancreas may cause disturbances in the digestion and absorption of the fats and proteins. The clinical signs of such disturbances may be striking, while the symptoms may be only slight.

Disturbances of the fat digestion result in insufficient absorption of fat, so that a greater percentage than normal is present in the feces. The stools may be oily, like butter, or of a gray asbestos-like color. The bulk of fecal matter is greatly increased.

This condition may be associated with considerable diarrhea, with resulting loss of strength, or it may persist for years without definite impairment in the health of the patient.

Disturbances of the protein digestion result in a marked increase in the percentage of protein in the feces. The stools may contain numerous undigested muscle-fibers. There results eventually considerable loss of weight on the part of the patient due to the lessened nutrition which he obtains from his food.

A striking impairment in the lipolytic and tryptic ferments

of the pancreatic secretion may be associated with the clinical condition of chronic pancreatitis. In the symptomatology of this disease the gastro-intestinal tract may play a conspicuous part. Dyspeptic disturbances are often a prominent feature, consisting of anorexia, discomfort from flatulence, offensive eructations, heart-burn, and nausea. Frequently there is a distaste for fats and meats. In the early stages of the disease constipation with flatulency is common, while in the advanced stage frequent bulky bowel movements, pale in color, offensive and oily, predominate. Very marked wasting of the patient is often a prominent symptom. There may be distinct tenderness in the epigastrium with some fulness above the umbilicus.

Adrenals.—*Addison's Disease.*—The gastro-intestinal symptoms in this disease are various. In the early stages of the disease patients complain of nausea, pressure on the stomach, and sometimes epigastric pains with vomiting. There is in the later stages generally a decrease in, or absence of, hydrochloric acid formation and ferment production. Diarrhea may alternate with constipation. Toward the end of the disease the diarrhea may occur in crises with great violence, without obvious cause, and be associated with spasms of the calves of the legs. It takes the form of frequent watery discharges with colicky pains, and may lead to rapid collapse, delirium, and coma. In the terminal stages there may be incessant vomiting. The abdomen is generally retracted and the abdominal walls tense, the pulse is small, and the clinical picture suggests that of peritonitis.

The Parathyroid Gland.—*Aparathyrosis.*—Of the clinical symptoms of insufficiency of the parathyroid gland, perhaps the most striking is tetany. With this condition slight or severe disturbances of the function of the gastro-intestinal tract are frequently associated. In one type the tetany develops in patients who have been sick for a long time with gastric and intestinal disorders, especially those producing high-grade stagnation of the stomach contents.

In another type the gastro-intestinal symptoms occur at or after the outbreak of the tetany. There is hyperexcitability

of the stomach musculature, increased secretion of the gastric and intestinal glands, and a pronounced "stratification" of the gastric contents.

In still another type the gastro-intestinal symptoms may occur later and be intensified by the occurrence of tetany.

The results of detailed studies show that in the acute stage of tetany the gastro-intestinal tract may show symptoms of hyperexcitibility and heightened tone, reaching eventually to a spastic condition. Associated with this is usually an increase in the secretory activity of the tract.

Diseases of the Pituitary.—Disturbances in function of the pituitary gland are not particularly associated with gastro-intestinal symptoms. Those which do occur are allied with hyperactivity of the gland function, as evidenced by the clinical condition of acromegaly. The gastric and intestinal symptoms in this disease are vague, consisting of increased appetite and thirst, constipation, and various ill-defined dyspeptic disturbances.

Secondary pressure effects from tumor of the hypophysis may cause cerebral vertigo, in which clinical picture nausea, with explosive, projectile vomiting may be very prominent.

Diseases of the thymus and pineal glands are not associated with any definite gastro-intestinal symptoms.

The thymus gland, through its correlation with the thyroid in hyperthyroidism, might be considered to play a part in the gastro-intestinal symptoms of Basedow's disease, but the association is, to say the least, a remote one.

Disturbances in the function of the pineal gland are likewise not often accompanied by gastro-intestinal disturbances. Only the local effects caused by enlargement of the gland with pressure upon the neighboring cerebral structures cause the gastro-intestinal symptoms. Here cerebral vomiting may be a striking symptom. The trophic changes produced by the gland are not associated with derangements of the stomach or intestines.

Discussion.—Though there are no specific disturbances of the gastro-intestinal tract associated with either the diseases of

metabolism or the ductless glands, except it be the diarrhea of hyperthyroidism, still a sufficient number of derangements of this tract do occur to make it of interest to bring them together for their diagnostic and prognostic importance.

When the etiologic chain of these obscure diseases is better unravelled, and the pathologic interrelationships more clearly understood, it may be that the rôle of the gastro-intestinal tract in these diseases will be clearer to the clinician. Until then it will perhaps have served a useful purpose to have gathered together the fragments of our knowledge on this subject in preparation for future clinical correlation.

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THE RÔLE OF DIET IN TREATMENT OF DIGESTIVE DISEASES

DIET is undoubtedly the most potent single therapeutic measure we possess in dealing with digestive diseases. The application of drugs is not to be compared with food properly prepared and given in a suitable manner, namely, essential caloric value combined with physical characteristics which will both tempt the patient and stimulate the psychic secretion of gastric juice, and at the same time so prepared (in the way of liquids, purées, etc.) that the minimum burden of physical and chemical endeavor is placed upon the damaged organs. One cannot emphasize too strongly the great importance of serving food which will cause the patient to anticipate with pleasurable expectancy the coming of the diet tray. Daily in our work are we more and more convinced of the efficacy of the versatility of nurse or doctor in their suggestion or preparation of food, playing a predominant rôle in restoring digestive organs and patients to vigorous physical fitness, after the former have been wrecked by injudicious eating and drinking so much in vogue today, which, in many cases, lead to a true anorexia or sitophobia, because of the abuse of what was once supposed to be an "iron stomach."

One must necessarily have a full understanding of the mechanical factors and physiology of digestion, also a fundamental conception of caloric value and chemical properties of the various foods, and last, but not least, digestive pathology. Without these primary sources of knowledge it obviously will not be pos-

sible to scientifically or practically apply dietetic principles in an intelligent and helpful manner.

It may be well to first discuss the physical characteristics of various foods: first, liquids; second, gruels; third, soft foods; fourth, solids.

Of the liquids, it may be well to divide them into non-stimulating (*a*) and stimulating (*b*) varieties. Of the former, we have—

(*a*) Milk, solution of egg-albumen, whey, cream, buttermilk, koumiss, kephir, cocoa, chocolate, malted milk, cream soups, *i. e.*, asparagus, celery, pea, etc.

(*b*) Beef extracts, beef juices, soups, bouillon, and broths of various kinds (chicken, beef, oysters, clam, vegetable). Coffee and tea.

Possibly it is best to speak of fruit juices as mildly stimulating.

Those foods which are next in consistency, tending toward the soft or solids, would consist of the watery carbohydrates, prepared from the finely divided cereals, or purée of vegetables, *i. e.*, oatmeal, cream of wheat, wheatena, hominy grits, cornmeal, malted milk, rice, macaroni, spaghetti, potato, vermicelli, spinach, asparagus, peas, cauliflower, beans.

Soft foods consist of cereals not diluted with milk or water —oatmeal, cream of wheat, wheatena, farina, hominy grits, Pettijohns, *purées* of spinach, peas, beans, cauliflower, asparagus, onions, potatoes. Purée of fruits—prunes, peaches, apricots, apples, etc.

Macaroni, spaghetti, vermicelli, and rice in their usual state may be considered soft articles of diet.

Tapioca, blanc mange, Spanish cream, gelatin, ice-cream, jellies, honey.

Eggs prepared in various styles.

Pulp of orange or grape-fruit.

Butter, cream cheese.

As solids in the strict sense we may consider poultry, fish, game, meat, potatoes, string beans, cauliflower, baked squash, beet greens, Brussels sprouts, turnips, carrots, cabbage, peas,

beans, celery, cucumbers, lettuce, parsnips, watercress, fruits, bread, cheese, nuts.

Now that we have specific knowledge concerning the various classes of foods—*i. e.*, liquids, gruels or mushes, soft and solid articles of diet—it will be of interest to consider other properties, because there are certain fundamental principles which must be thoroughly understood before we can acceptably prescribe the various articles enumerated above to certain and specific pathologic entities of the digestive tract.

While we have not included water as a food, yet its value is nevertheless thoroughly appreciated relative to the general and specific needs of the body. Therefore it will not be amiss to discuss briefly its rôle regarding the digestive tract. Many opinions have been advanced regarding the efficacy of drinking large or small amounts of water, but it seems that the wisest procedure is to consume moderate amounts (about 6 glasses) during the day, and, in addition (and this seems a point worth emphasizing), the intake should be evenly distributed. Large amounts at one time are certainly detrimental. A transgression of this last point is especially to be avoided in degenerative processes affecting the vascular system.

Always bear in mind the fact that practically no water is absorbed by the mucous membrane of the stomach, and, if the stomach is functioning normally, a pint will be evacuated in from one-half to three-quarters of an hour. The former point remembered will tell us why the patients with gastric stenosis bitterly complain of intense thirst. If taken in moderation water certainly does not retard digestion; in fact, it may be helpful inasmuch as it is a slight stimulant of gastric secretion, and also it may be of some value in softening food. As to its relationship to absorption, one would think, if anything, it would assist and not hinder.

Regarding mineral waters, especially those impregnated with carbonic acid gas, one may say if taken in moderation they are helpful, due to the promotion of chemical processes of digestion, because of an early and abundant secretion of gastric juice; also it may be helpful from a mechanical standpoint due

to the movements of the stomach being accelerated by the carbonic acid. These waters should not be used where heart affections are present, or where the appetite is already depressed.

Milk is one of the most valuable and important articles of diet which we possess. Because of the fact that it curdles with the formation of clot upon entrance into the stomach, many are inclined to class it with the solids; however, our personal experience (with few exceptions) has been so successful when using it in the sense of a liquid that we prefer not to look upon it in the ordinary sense of a solid. We are in agreement with Pawlow's statement that in proportion to the amount of nitrogen milk contains it requires for its digestion a weaker gastric juice than any other food. Hence the secretory work required of the stomach for its digestion is small; a point well worth remembering when we wish to prescribe it for a stomach whose digestive capacity has been weakened. At times when whole milk disagrees we find that skimmed milk will be well handled. This is possibly due to the fact that the fat which milk contains seems to have a restraining influence on the amount of gastric juice secreted, and it is also well to remember that when given by itself it is not nearly so completely absorbed as when it forms part of a mixed diet. The digestibility of the casein of cow's milk depends on whether it is precipitated in small or large clots, and we know that the latter may be avoided by the addition of lime-water, sodium bicarbonate, sodium citrate, and milk of magnesia, also hydrochloric or lactic acid, any of these substances combining with the casein tend to break up large clots; this is accomplished by interfering with the action of the rennet. Boiling milk tends to produce the same effect as just described, and, in addition, kills many bacteria. Undoubtedly casein is the great obstacle to easy digestion.

Hutchison is of the opinion that just as boiling does not appreciably diminish the digestibility of milk in the stomach, so it does not to any important extent interfere with its absorption in the intestine; further, it seems to be absorbed with less expenditure of energy than any other food, and also there is reason to believe that much of the value of milk diet and milk "cures"

in many cases is due to the diminished absorption of putrefactive products from the intestine which these bring about. Needless to say there are certain cases, notably those of colitis, which absolutely reject milk, the curds acting as a decided irritant. Here we may use the various alkalies or acids as suggested, also whey, or at times the addition of farinaceous material proves efficacious.

Milk is by no means a perfect food, but it is admirably fitted to supplement the deficiencies of other articles of diet. Cream, as everyone knows, contains a large percentage of fat, and is an excellent fuel. Butter is, of course, a mass of fat, closely compressed, and is the most easily digested of all fatty foods. It is almost completely absorbed in the intestine. Koumiss and kephir are sour milks, the former being fermented mare's milk, while the latter is a fermented product of milk from the cow. Buttermilk differs from cow's milk in that the percentage of fat is materially diminished, and this is probably the reason it is so much better handled in many cases than whole milk with a high fat content, and also the lactic acid bacilli are supposed to have a beneficial effect on the bacterial flora in a certain percentage of cases. It contains the casein of the milk in a finely coagulable form.

Whey, as everyone knows, is the fluid which is obtained from clotted milk, and supposedly has little nutritive value. Hershell and Abrahams deprecate the fact that whey has not received the attention due it, pointing out the fact that it contains the whole of the milk-sugar and the greater part of the salts and the soluble albuminoid matters of the milk. It may be well to remember this in cases that are unable to digest milk curd.

Cocoa and chocolate contain rather large amounts of fat, carbohydrates, and protein, and while not nearly so stimulating as tea or coffee, are more sustaining and quite nutritious. They are usually prepared with milk, and this adds to their nutritive value. One must not forget that they contain tannin, and are, therefore, to a certain extent astringent.

Cream soups manifestly are prepared from a fine purée of various vegetables, such as asparagus, peas, celery, etc.; the

addition of milk and cream renders them quite palatable and highly nutritious. They are extremely bland and non-irritating, and we find them splendidly received by many of the "weakling type" of stomachs.

Fruit juices contain the minimum of nutrition, and it is for flavor mostly that we ingest them. We have the various acids represented according to the fruit in question—*i. e.*, grape, tartaric; lemon, citric; apple, malic—these at times chemically stimulate bowel movement and often prove valuable adjuncts when used in conjunction with other agencies.

A most important factor possessed by daintily served fruit juices is the psychic effect on appetite, naturally often resulting in markedly improved digestion and nutrition. In many digestive cases our versatility in being able to handily and quickly introduce new and appetizing foods or beverages into the patient's diet will spell the difference between victory and defeat in our supervision of stubborn and prolonged dyspeptic conditions.

Beef extracts, beef juices, and the various soups and broths, contrary to popular opinion, contain very little nutriment, acting more in the capacity of stimulants. The beef extracts are prepared by chopping up meat, heating under pressure with a small amount of water, and the extract is filtered and evaporated. The stimulating properties are dependent upon the extractives of meat, and even this statement does not go unchallenged. However, Pawlow considers them the most potent gastric excitants we possess, and claims they stimulate appetite and aid digestion. It is claimed beef extracts accelerate gastric secretion, and it is a valuable addition to other food, but in themselves must never be considered of real value from a nutritive standpoint.

Beef juice cannot be classed as a real food because of the small amount of true nutriment contained therein. However, a larger amount may be used than of beef extract. The same may be said of beef-tea and the various broths.

Coffee and tea are stimulants and possess practically no nutrient qualities. They contain fairly large amounts of caffein

and tannin. As regards tea, when one wishes to avoid tannin to a great extent, care should be taken to infuse for a very short length of time. A cup of tea or coffee contains about the same amount of caffein and tannin—*i. e.*, about 1½ grains of the former and slightly over 3 grains of the latter. In the great majority of digestive diseases these beverages are certainly not to be recommended.

In passing, a few words may be said as to alcohol. It acts locally as an irritant, which accounts for the catarrhal condition that follows its continual use, especially when taken on an empty stomach. It causes marked secretion of gastric juice and saliva, and in moderation at times is helpful in digestive cases. Alcohol is quickly absorbed by the mucous membrane of the stomach, hence its rapid effect.

While alcohol is classed as a stimulant, this effect is transitory, as it is not favorable to producing sustained muscular effort. At times it is found advantageous to give light wines as an aid to digestion in those who are overworked or fatigued. In diabetes alcohol is at times useful as a real food—1 or 2 fluidounces may be taken daily. Wines tend to increase appetite and gastric secretion, and in moderate amounts may prove beneficial. In some wines the acid content is high, and these should not be prescribed in gouty or rheumatic conditions.

We may now consider cereals as a whole. These preparations are manufactured mostly from corn, wheat, rice, oats, and barley. The chief characteristics of this type of food is the large percentage of carbohydrates they contain. Some may be slightly richer in protein and fats, as oats and rye, while corn has rather a high fat content; wheat and rye have a large amount of protein and a moderate amount of fat.

Cereals are valuable as foods, and enter largely into our dietaries in the treatment of various digestive diseases, as will be noted later. As cereals we may mention oatmeal, cream of wheat, hominy grits, cornmeal, corn flakes, etc. Macaroni, spaghetti, vermicelli, rice, and grits may also be put into this class of foods. These articles leave small residues, and are of especial value where good absorption is desired.

Vegetables form another important item in our dietary assets, and are generally divided into roots, tubers, green vegetables, and fungi.

The white potato is rich in starch, and contains a small amount of cellulose as compared with the various green vegetables. If cooked after being peeled they lose much of their nitrogenous constituents and mineral salts, which results in a diminution of their nutritive value, therefore the cooking process should be done in their "jackets." Their digestibility as regards stomach and mouth depends on the form in which they are eaten—the purée being most easily handled, and the mealy more easily digested than the waxy (especially the new variety). In the intestine the potato is well absorbed owing to the small amount of cellulose, hence it is not of great value in sluggish intestinal conditions.

There is not a great difference between the composition of sweet potatoes, yams, and white potatoes, except that the former contains about 4 to 10 per cent of sugar. We may say that they are fairly digestible.

The various roots, such as parsnips, salsify, carrots, turnips, beets, onions, contain a large percentage of water and varying amounts of carbohydrates, the latter much less than that found in the potato, while the fiber is greater. These articles are not of great value from a nutritive standpoint, but assist greatly in balancing the diet, also their fiber materially helps in forming the ballast necessary for the proper stimulation of intestinal peristalsis. On account of the cellulose contained they are often not well borne, especially in irritable conditions.

We group in the green vegetable series cabbage, celery, cauliflower, asparagus, spinach, lettuce, cucumbers. They, of course, offer a rich supply of organic acids and mineral salts, and, while the amount of nutriment as compared with their bulk is not great, yet it is sufficient to be of use; also the cellulose, of which there is a large percentage, is of inestimable value in stimulating the movement of the intestine, and at the same time promoting a secretion of fluid contents from its walls. Constipation, with its often accompanying sluggish liver, is greatly helped by these

products. The purées of these vegetables are often wonderfully helpful in various irritative conditions.

The digestibility of green vegetables naturally depends upon the amount and character of the cellulose, the older ones naturally having tough fibrous tissues, while the young greens are tender and soft. In irritable conditions and very atonic states, especially the latter, which often occur in older people, the tough fibrous vegetables are not well borne.

In many of these types of cases it is essential that they should be put upon a well-balanced diet, and one of the requisites is vegetable articles added to the other food. This is easily accomplished in the majority of cases by preparing vegetable purées; they can be made highly nutritious and palatable. The vegetables are cooked (preferably by a fireless cooker for several hours or in a steamer), mashed to a pulp, then rubbed through a sieve, butter or cream added, then put in a saucepan and thoroughly heated. In handling hundreds of cases we have found these purées to be most efficacious.

Raw vegetables, such as tender celery, lettuce, watercress, and finely shaved cabbage made into cold slaw are often very well borne. To them may be added olive oil and a small amount of salt.

The patient should always be cautioned to masticate slowly and thoroughly, and, if the advice is heeded, they will be well borne in the vast majority of cases.

Relative to purée of potato, remember there is a marked difference between the mealy part of baked potato, or that which is mashed, and properly made purée. To prepare the latter, boil or bake, rub through a sieve, then beat up with cream or milk, add a small amount of butter, put in a saucepan, heat, and it is ready to serve.

Dried legumes or pulses—dried peas, navy beans, lima beans, soy beans, peanuts. Their chief value lies in the fact that they have a high nitrogen content in addition to carbohydrates. They are quite hard to digest, not being well acted upon by the gastric juice. The most satisfactory way to serve the legumes is by soaking over night, thoroughly cooking, mashing, and press-

ing through a sieve. There is an abundant amount of sulphur in peas and beans, and when they are decomposed, hydrogen sulphid is evolved, this accounting for the marked gaseous distention which often occurs after their use.

The fungi, mostly represented by mushrooms and truffles, enter very little into the subject of dietetics in disease. They contain a large percentage of cellulose and are hard to digest.

Fats, in the forms of butter and olive oil, are the most valuable varieties, and, on the whole, are easily assimilated. It has been reckoned that $5\frac{1}{2}$ ounces of butter can be easily absorbed with slight loss. We must always combine it with other food, as it is not well borne when administered alone or in large quantities. We often prescribe $\frac{1}{2}$ pound a day, and find it easily digested, being a most valuable adjunct in fattening rest cures.

Fats and oil should be forbidden in acute digestive disorders —diarrhea, obesity, gall-stones, and gastric dilatation.

Bread is characterized by a large starch content, and naturally a certain amount of digestion takes place in the mouth. The more thoroughly bread is masticated, the more complete will the conversion of starch be. Toast, crisp crackers, and biscuits are much easier to pulverize than bread, and because of the thorough and continued chewing necessary a large amount of saliva is called forth, thus making another potent factor in the process. One must not forget the reflex and psychic production of gastric juice from this procedure. Fresh bread is hard to chew and does not allow of thorough absorption of the saliva; further, it is resistant to the action of gastric juice. In the intestine absorption of white bread is marked by its thoroughness; however, the proteins are proportionately not nearly so well absorbed as those of meats. Bread is not unlike milk in one attribute—it apparently is better absorbed when combined with other foods. Brown and whole wheat breads contain more bran than the white, and because of the increased amount of cellulose contained are not as completely absorbed in the intestine.

Bread is certainly one of our most nutritious foods. One

must remember that three-fifths of it consists of solid nutriment and two-fifths water—a ratio approached by but few articles of diet.

As with milk, so it is with bread—a splendid nutritious food, but not complete—therefore the best results are obtained by supplementing it with other substances.

Meat is composed of muscle-fibers, connective tissue, fat—the comparative amounts of each differing in the species of animal, poultry or fish, and the various cuts. A large amount of fat may serve to diminish the digestibility of the meat.

From what has been said it is obvious that protein and fat are the chief constituents of the above foods, but one must remember that water enters largely into the composition of meat. It is of interest to note that cooking diminishes the amount of water in meat, resulting in an increase of its nutritive value, but at the same time tends to lessen the digestibility, hence it is best to serve underdone meat to weak stomachs. As to the comparative digestibility of the various meats there is a difference of opinion, but veal and pork are probably the most indigestible; however, one must never lose sight of idiosyncrasies possessed by various people. The breast of chicken and game is especially well digested, and we know that meat as a whole is quite thoroughly absorbed in the intestine, leaving little residue. It is our source from which building material is obtained for the body, also one of its attributes is that it has a stimulating effect, and Hutchison is of the opinion that the feeling of well being which follows a meat meal may be put down to this cause. The amount of fat contained in various meats is of fundamental importance regarding their nutritive value. Liver, kidney, and sweetbreads have a high nucleoprotein content, and are often eliminated from the diet, especially in the case of those of a gouty diathesis. Sweetbreads, however, are easily digested.

As regards fish, there is nothing of especial moment to discuss. Like meat, the chief constituents are protein and fat, the former, of course, dominating to a great extent—salmon, salmon trout, mackerel, turbot, and herring contain the largest

amounts of the latter. Fish contains more gelatin and fewer extractives than meat. Their absorption is quite complete, and they are very nutritive, the degree of the latter depending on the amount of fat. Of oysters, there is not much to say. They contain a small amount of protein, fat, and carbohydrate, consequently are not very nutritious, but easily digested and absorbed quite completely.

The chief constituents of cheese are casein and fat. Examples of the hard variety are Edam, Cheddar, Roquefort, soft, Stilton, cream, Camembert, Brie, and Neufchatel. The stomach is unable to digest the cheese, but after its entrance into the intestine not much difficulty is encountered—it is thoroughly absorbed. The reason for the difficulty of digestion lies in the fact that cheese contains a large percentage of fat, and this prevents the gastric juice from gaining access to the casein. A given quantity of cheese yields a much greater number of calories than the same amount of meat. Our experience is that the soft cream cheese is the most digestible of all varieties.

Eggs consist of the white and yolk, the latter being its most nourishing portion. They contain rather good amounts of protein and fats, practically no carbohydrates. Lime, iron, and phosphoric acid are the most important mineral constituents. Eggs are quite easily handled by the stomach, the soft boiled leaving it in the shortest time. If a hard-boiled egg is finely divided and thoroughly masticated it is disposed of as well as the soft boiled. We find at intervals patients who have a true idiosyncrasy toward eggs, and many times they cannot be taken. They are easily digested in the intestine and leave little residue. Their nutritive value is due almost entirely to protein and fat.

It cannot be said of fruits that they are of great nutritive value. However, the greater part of nourishment which they do contain is present as the carbohydrate group, and a large percentage of this is in the form of sugar, usually levulose, although apples, apricots, and pineapples also have in them cane-sugar. Cellulose is present in all fruits, but necessarily is rendered quite soft and more digestible by the cooking process.

One must remember that the mineral constituents—*i. e.*, potash combined with tartaric, citric, and malic acids—at the end of the metabolic process render the blood more alkaline and the urine less acid. Fruit which has not thoroughly ripened, thus having a greater amount of hard cellulose with excess of acids, is not well digested, and the latter often prove irritating to the digestive tract. If the ripening process has been allowed to go to maturity, the more moderate amounts of cellulose and acids often act as mild stimulants, mechanically and chemically, upon the intestinal wall, often greatly assisting a sluggish bowel. (It may be well to state at this time that here, as in other discussions of the various articles of diet, for the precise percentages of protein, starch, fats, etc., the reader is referred to standard text-books.)

Nuts are of high nutritive value because of their richness in protein, fat, and carbohydrate, but are quite indigestible, due to the high fat and cellulose content. While thorough mastication will overcome this to a certain extent, it is more satisfactory and effectual to have them artificially ground. The various butters and preparations made from nuts are highly nutritious. It is interesting to note that they closely resemble meat in their general make up, and are even a more concentrated food than cheese.

Sugar is a most important article of diet, and some valuable deductions may be succintly put by quoting from Hutchison:

"Sugars in the stomach tend to undergo fermentation.

"I. Alcoholic, resulting in the production of alcohol and acetic acid.

"II. Butyric, with the formation of butyric acid.

"III. Lactic, the product being lactic acid.

"Practical deductions:

"I. In dyspepsia the absorption of carbohydrates is delayed, and therefore all sugars tend to ferment.

"II. In dyspepsia with lactic acid formation one should avoid dextrose, levulose, and invert sugar, and use cane-sugar, maltose, and lactose in moderate amount.

"III. In butyric fermentation lactose should be preferred.

"IV. In alcoholic and acetic fermentation one should forbid invert sugar and levulose, and give lactose.

"It will be observed that of all sugars, lactose is least liable to fermentation. This is another point in favor of the value of a milk diet in stomach complaints."

However, from practical experience, we see that if sugar is taken in moderation with other foods it is, in the great majority of cases, well handled. In contradistinction to meat, sugar is probably the chief source of muscular energy.

Spices and condiments probably act reflexly through the organs of taste, and also may have some direct action upon the stomach itself in calling forth a secretion of gastric juice—they act as irritants, and are contraindicated in ulcerative or irritative lesions of all kinds. Mustard, pepper, vinegar, nutmeg, allspice, cinnamon, and cloves may be considered examples of spices and condiments.

Of desserts, we may mention gelatin (in most cases with cream added on account of nutrition), custards (boiled or baked), blanc mange, jellies, tapioca, Spanish cream, ice-cream, etc.

With the exception of gelatin the above-mentioned articles markedly resemble one another in composition. Gelatin is considered a protein sparer, and the calf's foot jelly as purchased contains about 4.3 per cent. of protein and 17 per cent. of carbohydrates. It is easily digested and has the capacity of fixing a large amount of acid—hence its efficacy in hyperacid conditions. The other preparations are made with sugar, butter, eggs, milk, and salt, therefore their intelligent application in various conditions would depend on our knowledge of the different percentages of the individual ingredients.

Recapitulating for a moment, it will be noted that we have discussed the various fundamentals with which we should be familiar—the types of food and their individual characteristics. We are now prepared to apply our knoweldge in a practical manner to the diseased condition of the digestive tract. It would manifestly be impractical to discuss separately the many diseased conditions of each digestive organ. therefore it seems

best to deal with the subject in a general but at the same time detailed manner.

We shall first deal with ulcerative lesions, and at this moment one must have in mind the underlying pathology and anatomy of the part in question.

In beginning the diet in these cases, bland, non-irritating, and, as far as possible, nourishing liquids should be given, so that the minimum amount of endeavor is brought forth from the affected organ. We now refer to the list of such articles, and find milk and egg-albumen stand at the head. In starting liquid diets remember to give them in small amounts (1 to 3 ounces) frequently repeated (one to two hours), depending upon the patient's ability to handle them. Here let it be pointed out that the ironclad following of text-books in giving ulcer cures—*i. e.*, adhering to amount, hour of administration, number of days such and such an article is kept up, etc.—is most pernicious, and a little later we will discuss how each practitioner can intelligently and correctly judge for himself in the vast majority of cases just when to increase the dietary. If milk is not well borne, then remember the advice given regarding the addition of various alkalies, also the use of skimmed or parboiled milk, whey, albumen, buttermilk, malted milk (fruit juices are often well tolerated). One will note that cream soups, cocoa, and chocolate are included in the bland, non-irritating liquids. However, it will be well to administer these later when the stomach is handling other food in a satisfactory manner, and at a time when we are especially desirous of increasing weight, for in the weakened state of digestion we often find fats not well tolerated.

When we wish to increase the amount and change the consistency of nourishment slowly, we simply advance to the gruels and mushy foods—watery gruels of strained oatmeal, farina, cream of wheat, hominy grits, cornmeal, vermicelli, rice, purée of potato, spinach, asparagus, peas, and cauliflower. These watery carbohydrates call forth the smallest amount of gastric juice, therefore causing the slightest efforts to be brought into play by the stomach. Smithies very aptly suggests flavoring

the above with coffee, chocolate, vanilla, and caramel, also adding small quantities of arrowroot or cornstarch in order to produce a thin emulsion.

If the digestive apparatus is not burdened by the above class of nutriment, then access may be had to those of a degree nearer solids—the soft cereals in what might be termed their native state—oatmeal (best strained), farina, cornmeal mush, hominy grits, cream of wheat, etc.

Eggs in very soft states, as boiled, scrambled, poached, raw, or well beaten in milk.

Small amounts of cream soups may be tried.

Purée of vegetables, as mentioned above.

Purées of fruits, fruit juices.

Toast (stale, sliced thin, and thoroughly dried out in a slow oven), crisp crackers.

Cream cheese.

Butter.

Beverages may be selected from those mentioned above.

Soft desserts.

If we now again wish to advance our line of diet, the following general dietary may be applied (from lists noted above):

Cereals, eggs (all styles except fried), cream soups, potatoes (baked or well mashed), rice, macaroni, spaghetti, asparagus, spinach, tender string beans, Brussels sprouts, peas and beans, cauliflower, onions, creamed carrots, turnips, beet greens, baked squash, rhubarb, lettuce. (It is safer to continue the fibrous vegetables in purée form for some time.) Toast crackers, crisp upper layer of corn bread. Milk, buttermilk, malted milk, cocoa, chocolate. Stewed fruits and their juices, soft part of baked apple, apple float, prune whip. Cream cheese, butter. Light desserts, including well-made rice or bread pudding. Raw fruit, such as apples, peaches, and pears, are usually not well borne. Meats should be the last articles of diet to be allowed—tender breast of fowl, lamb, rare hamburger steak or beef, fish (boiled or baked), soft part of oysters. None of those mentioned should ever be fried, and should not be allowed under three to six months.

An admonition was made as to avoiding hard and set rules for increasing, decreasing, or applying new articles of diet. How may everyone become efficient in this regard? There are four points: (1) Subjective symptoms of patient—nausea, pain, discomfort, etc.; if these are markedly ameliorated, it is time to consider increase in diet. (2) Objective—tender points, muscle spasm, pain on pressure, vomiting, melena, and general appearance; an improvement in these likewise should be of value in pointing the way to progressive measures. (3) Microscope—stool examinations to determine if various food-stuffs are being digested, also if mastication has been complete. (We can often in this manner keep a good check on one who slights mastication, bolts food, and then wonders why he does not improve.) (4) Stool—investigation for occult blood, note intensity of reaction, and then watch for diminution and final disappearance. A careful study and résumé after close analysis of the information obtained by the above methods will enable us to intelligently know just about the time to make the necessary changes.

The above principles of treatment may be applied to ulcerations of esophagus, stomach, intestines, in spastic states of these organs from reflex conditions, such as pylorospasm from chronic appendicitis, gall-bladder, duodenal ulcer, etc.

Let us see how simple it is to apply dietetic treatment to acute inflammatory conditions of the digestive tract. We must always consider first the pathology, and from this we will learn whether bland, non-irritating substances and those leaving little or no residue are indicated, or, on the other hand, foods which from mechanic, chemic, and thermic stimulatory standpoints are to be used. We have learned that all tissues showing acute inflammatory reactions should not be stimulated, but rested; therefore after the preliminary evacuation of gastric and intestinal contents by the various methods, followed by a period of starvation, we apply liquids of a bland, non-irritating variety, it is not essential that they should be extremely nourishing in the acute cases; therefore we refer to our list of non-irritating fluids; probably the safest one to try is egg-albumen, and this may be given in fruit juices; if well borne, gradually en-

large the number and amount of the various liquids. Attention should be called to two points. One is that at times in gastric and intestinal acute upsets milk is not well borne, therefore, if given at all, it should be well diluted, skimmed, parboiled, or alkalies added. The second point, although the broths are classed as stimulating, they need not be irritating, they leave no residue, and if well diluted often act splendidly. From these we graduate to watery carbohydrates, soft purées and cereals, soft eggs, custards, toast, and on through the list, until we finally enter again upon a good substantial diet, and again, at the expense of being monotonous, add meat as the last article. A practical point may be enumerated—when you do give meat, start on scraped (not chopped) beef, for here we have only the tender muscles without connective tissue. Make this into cakes and slightly broil; succeed this by breast of fowl, and later meats in rare state passed through a food chopper, before returning to meat in its natural form. The latter would be a splendid procedure to follow with the more mature and high cellulose content vegetables.

The pathologic conditions which may be successfully handled by the above methods are acute inflammations of esophagus, stomach, small and large intestines from the various etiologic factors.

As a sequel or result of the above processes we meet at various times the chronic inflammatory states, which may be of benign, malignant, leutic, or tubercular origin. Almost needless to say the pathology here met with is quite different from that just discussed. While the inflammation is chronic, yet we must bear in mind it is not restored to normal by keeping up a continued irritation, therefore we should apply food which, while non-irritating, yet, because of various properties, acts as a mild stimulant, coaxing, as it were, a diseased organ back to the normal. Here again we avoid heavy articles which may cause mechanic, chemic, or thermic irritation, and in lieu of these we transform these very foods into benign, moderately stimulating and helpful, health-restoring mediums. You ask how? We merely refer you to soft cereals—eggs, various purées (vegetable)

—not forgetting to especially call your attention to the fruits as purées—*i. e.*, apple float, prune whip, and the like, toast—hard? Yes, but earlier we have pointed out how, if care and attention is directed to thorough and painstaking mastication, a soft mass thoroughly impregnated with saliva is produced, calling forth not only splendid salivary secretion, but, in addition, a reflex gastric flow, thus preparing the stomach to receive the soft minutely comminuted food. This is a point well worth emphasizing. Now graduate your diet up through the various grades, and you will have solved the problem of chronic inflammations.

Just a word as to mucomembranous colitis: In this condition the spasticity of the gut with some degree of inflammation are the causative factors producing quite often, among other symptoms, obstinate constipation. Our object is to give mild stimulating food in finely divided states and nutrient in effect—soft cereals, carefully prepared purées of vegetables, and fruits (apple, pear, plum, apricot, prunes), spaghetti, macaroni, vermicelli, well-boiled rice with the soft desserts, milk puddings of tapioca, sago, rice, cream soups, toast, crisp crackers make an ideally suitable menu. Later chicken and beef, prepared as described earlier, may be cautiously added. Use the microscope, and if only a few, well-rounded, non-striated muscle-fibers are noted, then we may forge ahead with some temerity, but if they are sharp on ends, many in number, and well striated, we know digestion is incomplete, and it is time to consider a retrenchment. In the early treatment beef extracts and juices should be withheld also, as pointed out above. The safest procedure is to start with bland, well-divided, non-irritating, farinaceous material, cautiously working up to the vegetables, etc.

Some authors use a diet diametrically opposed to the above advice, and give coarse green vegetables, coarse fruits, and meats. This may be followed, but our personal feeling is that the soft, non-irritating form of food forms a more rational line of treatment.

Regarding diet in various stenoses—esophagus, stomach,

intestine—one finds here an easy and simple discussion. The spastic variety is handled in identically the same manner as the first and second stages of ulcer, *i. e.*, bland liquids, followed by finely divided, farinaceous foods, then purées. Just a word as to change from purées to solids—go very, very slowly and exert the utmost caution relative to meat even in the finely divided state.

It may not be amiss to state, what is known to every medical man, organic stenosis is fundamentally surgical in the vast majority of cases; however, if we wish to treat it dietetically, our opinion is that the soft, moist purées are better borne and more effectually dealt with by the stomach than heavy foods or large amounts of liquids; therefore after the stomach has been thoroughly lavaged, small, frequently repeated meals consisting of the foods just mentioned are far preferable to large meals at long intervals. Excesses of farinaceous and fat foods should be avoided on account of fermentation. The character of lesion, be it benign, malignant, tubercular, or luetic, has no bearing on the application of the above principles.

Acute appendicitis after the starvation period is dieted according to the methods enunciated in acute inflammatory ailments.

Chronic appendicitis often results in reflex pylorospasm, ulcer, and spastic constipation; therefore reference to these states will supply all necessary knowledge concerning this pathologic lesion.

Hyperchylia gastrica and hyperchlorhydria are symptoms and not distinct disease entities. They result from intrinsic and extrinsic lesions, such as gastric ulcer, inflammations, duodenal ulcer, chronic appendicitis, gall-bladder involvement, etc. When the diagnosis has been made, treat the offending organ. Also it will be well to caution that it is best to restrict the use of bread, potatoes, sugars, and all sweet and sour articles of diet in these ailments.

Two conditions often met with which interest us clinically and dietetically are protein putrefaction and carbohydrate fermentation. In the former eliminate protein of all character

and give the green vegetable and fruit purées, then farinaceous purées, etc., gradually working up to general dietary, including meats, for here we usually have a marked derangement of normal intestinal capacity; add very minute (finely divided in food chopper) amounts of tender breast of fowl, lamb, etc.; intensely scanning stools with microscope and closely watching reaction with litmus; also noting color and general consistency. In the latter condition (carbohydrate fermentation) all carbohydrates are withdrawn, and a protein-fat régime inaugurated—finely divided meats, fish, soft part of oysters, meat broths, butter, eggs. There is such a small amount of carbohydrates in well-cooked and puréed green vegetables that the latter are usually allowed—*i. e.*, asparagus, spinach, cauliflower, carrots, peas, squash, celery, beet tops, etc. When these are well borne, experiments may be tried with very small amounts of white potato, bread, rice, etc.

In achylia gastrica again we think of the pathology of the part—attenuated, atrophic glands in many cases, absence of digestive juices, gaping pylorus, slight reflex stimulation of pancreatic and liver secretions; hence the food as received in the stomach is passed on to the intestine. Manifestly then the diet should be taken in such a state as to throw the slightest burden in every manner upon the stomach and intestine. This is accomplished by bringing into use soft, farinaceous foods, cereals, eggs, purées of vegetables and fruit, toast, crackers, butter, cream cheese, light desserts. If meat, fowl, or fish are allowed, it should be given in scraped or finely divided form. Milk (variously prepared) and buttermilk are usually well borne, and cocoa, chocolate, weak tea, or coffee may be tried.

Pancreas: The conditions in the intestine in disease of this organ are very similar to those found in achylia, and if the power of all enzymes are diminished or absent, it means there will be a great decrease in the digestive action of the intestinal juices. The only way then—from a dietetic standpoint—to deal with such a weakened digestion is to make its duties less arduous. This is accomplished by following out the same rules made use

of in achylia, working back, of course, to approximately a normal diet as soon as the functions of the organ will permit.

Liver: The same diet may be applied here as in the chronic inflammatory conditions of the stomach and intestines, as ofttimes both are due to the same etiologic factor; food should be well divided and non-irritating, especial care being taken to avoid fats and rich food, also sugars and carbohydrates.

As regards gall-stones, practically all authors are agreed that small, frequently repeated meals are preferable to large and infrequent ones, as it is generally agreed that the discharge of chyme from the stomach greatly increases the flow of bile into the duodenum, due to a reflex mechanism dominated by the law of contrary innervation.

Large amounts of water should be insisted upon.

Constipation: We generally have one or two types to deal with: (1) Atonic, (2) spastic. In the former a stimulating diet, such as the following, is to be recommended:

Oatmeal (2 or more heaping teaspoonfuls of bran), Pettijohns (25 per cent. bran), shredded wheat (cream may be added to cereals), various fruits (raw or stewed), apples, pears, dates, figs, etc.; also fruit juices, green vegetables, spinach, celery, lettuce, cabbage, Brussels sprouts, etc.; whole wheat, bran, graham breads; honey, marmalade, molasses; buttermilk, cider. Small amount, if any, of meat. Avoid tea, coffee, red wines, cocoa, chocolate.

It is often found advantageous to take one or two glasses of water (hot or cold) every morning on an empty stomach in an endeavor to inaugurate peristalsis.

The spastic type is treated by using practically the same articles of diet, except they are given in the finely divided state. One can generally follow the means mapped out in mucous colitis.

In conclusion it may be well to discuss a few odds and ends.

Very often we are asked to outline for a ptaient who has recovered from one or more of the previously discussed ailments a table containing suggestions for a well-balanced diet. The following may serve this purpose:

Breakfast: Fruit—orange, grape-fruit (one-half).
Saucer cereal and cream, or soft eggs.
Roll or slice of toast—buttered.
Cup Kaffe Hag, Postum, or milk flavored with coffee.
Sugar (not over one lump).

Lunch: Cup of clear broth.
Small baked potato.
Helping green vegetable.
Saucer stewed fruit.
Roll, Graham, bran or whole wheat muffin.
Cup weak tea.

Dinner: Cup cream soup.
Chicken, fish, lamb chop, beef.
Baked potato, rice, macaroni (one choice).
Lettuce salad.
Bread as above—Uneeda or cream lunch cracker.
Butter.
Light dessert as per suggestions above, with small amount of American or cream cheese.
After dinner cup Kaffe Hag or some coffee substitute.

Generally speaking, articles to be avoided are pepper, mustard, vinegar, condiments of all kinds, rich pastries, pickles, gravies. Abstain from excesses of bread and potatoes, sugar, and sweet things. As to alcohol, the safest course is to eliminate it entirely.

If with the above we wish to suggest intermediate feedings, the following may be brought into play: Cup of broth or cream soup with several buttered crackers, cup custard, blanc mange and the like, milk, buttermilk, milk-shake with egg, or any of these combinations served in an appetizing manner. They may be taken between meals and at bedtime.

Always remember that certain people have marked idiosyncrasies regarding particular food-stuffs; therefore it is wise to bear this point in mind.

In chronic cases do not keep upon soft, sloppy food longer than absolutely necessary. Our experience has been that if food is repugnant to patients it is much better to substitute other varieties even though in some respects it is contraindicated. The psychic factor undoubtedly plays a major rôle.

In nervous, dyspeptic, or functional conditions, treat symptomatically, and as soon as possible put upon a good general dietary, such as that just suggested. These cases should not be pampered dietetically.

CLINIC OF DR. ELMER B. FREEMAN

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ESOPHAGOSCOPY AS AN AID IN THE DIAGNOSIS AND TREATMENT OF ESOPHAGEAL DISEASE

Introduction.—In presenting this Clinic on Esophagoscopy I desire to very briefly review the early literature on the subject; to mention the indications for and the contraindications to esophagoscopy; to describe the method of examination and to discuss esophagoscopy as an aid in the diagnosis and treatment of esophageal disease.

Early Literature.—The French were the first to call special attention to the passage of a tube down the esophagus. M. Baillarger in 1845 wrote a very interesting article on catheterization of the esophagus, and called attention to the fact that for years Esquirol had been using a sound of elastic gum passed through the nares into the esophagus through which liquids were introduced into the stomach. This method was only employed in feeding lunatics who refused to take nourishment. John Aylwin Bevan in 1868 called the attention of the profession to the use of an esophagoscope for the removal of foreign bodies. The instrument he used was 4 inches long, $\frac{3}{4}$ inch in diameter, and illuminated by a light reflected from a mirror. In 1881 J. Mackenzie described a skeleton tube which was introduced into the esophagus while flattened, and by an attachment on the handle the tube could be opened and the esophagus dilated. Killian ascribes to Kussmaul the first esophagogastroscopy in Germany, and the practical solution of the problem to Von Hacker in Austria. Einhorn was the first to do esophagoscopy in America, and he was followed by King, Ingals, Coolidge,

Johnston, Janeway, Yankauer, Mosher, Stillman, Chevalier Jackson, and others.

Indications.—The indications for esophagoscopy are the presence of a foreign body in the esophagus and all other conditions in which there are discomfort, pain, or difficulty in swallowing.

Contraindications.—The contraindications are aortic aneurysm, cardiac disease with hyperthrophy, arteriosclerosis with hypertension, advanced pulmonary tuberculosis, cirrhosis of the liver and curvature of the spine (in the cervical or dorsal region), but these are not contraindications if the esophagoscopy is being done for the removal of a foreign body.

Method.—Before an esophagoscopic examination the patient should have a preliminary physical examination, and frequently an *x*-ray study to exclude contraindications.

Children under six years of age very frequently can be examined without the use of an anesthetic. The child is wrapped in a sheet, placed on the table in dorsal position, and firmly held by two assistants. If for any reason an anesthetic is necessary, a general anesthetic should be used and the preference given to ether. Local anesthetics are very dangerous in children, and the deaths which have occurred under general anesthesia have been when chloroform was used.

In adults the examination can always be made by using a local anesthetic except in cases of the removal of very large foreign bodies where it is necessary to give ether to thoroughly relax the patient.

My routine has been as follows: The patient is seated on a low stool, the head held by an assistant, in almost complete extension, and three or four applications of 10 per cent. solution of cocain (on cotton applicator) are made to the laryngopharynx; then the esophageal speculum is introduced, and, if necessary, two or three applications of cocain are made to the right pyriform sinus and the upper end of the esophagus. Before the esophagoscope is passed the esophageal speculum should be introduced and a careful inspection made of the pyriform sinuses and the upper end of the esophagus. By doing this we frequently find

diseased conditions which might otherwise be overlooked. The esophageal speculum is now passed through the right pyriform sinus and the larynx is gently brought forward; this brings into view the slit-like opening of the esophagus. The right pyriform sinus is selected because the esophagus in its downward course passes slightly from right to left, making it very much easier to enter the esophagus through the right pyriform sinus. The esophagoscope should be passed without the obturator, as this gives a better opportunity to study the esophagus. When the instrument is introduced to the cricoid region it meets with more or less definite resistance. This is caused by the contraction of the inferior constrictor muscle of the pharynx; this resistance is quickly overcome if a slight degree of pressure is used. After the cricoid region is passed in a normal esophagus there is no difficulty in passing the tube down to the cardia. There are four regions in which a normal esophagus shows narrowing of the lumen: first, cricoid; second, crossing of the arch of the aorta; third, crossing of the left bronchus; fourth, at the diaphragm; these are respectively 16, 23, 27, and 37 cm. from the incisor teeth. The cervical portion of the esophagus is a collapsible tube, the dorsal portion remains open, showing a slight dilatation during inspiration and a slight contraction during expiration. The mucous membrane is soft, smooth, and has a pale pink tinge which changes to a reddish hue at the cardia.

The esophagus is to be studied during the withdrawal of the tube as well as during the introduction, for in some cases a better view is obtained while the instrument is being withdrawn. The conditions in which esophagoscopy aids in the diagnosis are carcinoma, cicatricial, spasmodic, and pressure stenosis, ulceration, and diverticulum.

Carcinoma.—In malignancy the esophageal picture varies with the duration of the disease. Unfortunately, we do not see most of these cases until the disease is quite far advanced, for the patient does not seek relief until obstructive symptoms have occurred, and these are only found late in the disease. The upper portion of the esophagus should be examined with the esophageal speculum and the examination completed with the

esophagoscope. In my own experience I have seen more cases in the upper than in the lower and middle third of the esophagus. In making these examinations one is impressed with the inelasticity of the esophagus, which gives a sensation of firmness to the esophageal wall, also with the small amount of dilatation above the growth. The inelasticity of the esophageal wall is due to the cancerous infiltration, and the small amount of dilatation is due both to the infiltration of the esophageal wall and to the obstruction occurring late in the disease. In cases where the growth is submucosal it is quite easy to pass the diseased area unnoticed; however, in most of these cases there is a bulging of the esophageal wall with a sensation of hardness or firmness when the tube is passed. Jackson calls attention to white patches in the mucous membrane which look precisely as though the mucous membrane had been burned with silver nitrate. He believes that these patches may be the manifestation of early malignancy, and claims that they cannot be diagnosed in the endoscopic picture from luetic lesions. In the more advanced cases the growth has a polypoid appearance which may or may not have undergone ulceration. If the growth is ulcerated the border of the ulcer is irregular and the surface bleeds very easily. While making the examination it is very easy to remove a specimen with a cutting forceps for microscopic study, and this should always be done if there is any doubt in regard to diagnosis.

Cicatricial Stenosis.—Most of these cases are the result of the healing of ulcers produced by swallowing corrosive poisons; some, however, are caused by the healing of ulcers associated with tuberculosis, lues, acute infectious diseases, and after the removal of foreign bodies. In my own experience in the corrosive cases the stenosis has occurred in the middle and lower third of the esophagus; in tuberculosis and lues, in the upper third; cases associated with acute infectious disease I have not seen, but Jackson and others have reported quite a number. Jackson especially calls attention in the typhoid cases to the stenosis occurring in the cricoid region. It is only found in the very toxic cases, and is thought to be due to the healing of an

ulcer produced by the cricoid pressing the esophagus back against the spine. Cases that occur after the removal of foreign bodies are most frequently found in the upper third of the esophagus because most foreign bodies lodge in that location; but recently I have seen one case in which Dr. Johnston of Baltimore had removed a foreign body from the middle third of the esophagus two years previous to my examination; this patient complained of marked difficulty in swallowing. The esophageal examination showed a slight degree of stenosis. The esophagoscopic picture as presented through the esophagoscope varies with the degree of the stenosis and the period of time that it has existed. In cases of moderate-degree stenosis the scar tissue is not extensive and there is very little dilatation above the stricture, but the mucous membrane shows some evidence of chronic inflammation.

In cases in which there is almost complete stenosis the endoscopic picture is very different, the scar tissue is quite extensive, and may almost completely encircle the esophagus; there is definite dilatation above the stricture, which gives the esophagus a characteristic funnel-shaped appearance, and in the dilated portion there are chronic inflammatory changes of the mucous membrane with superficial ulceration. In cases of complete stenosis the scar tissue is so extensive it completely excludes the esophagus.

Spasmodic stenosis of the esophagus probably occurs more frequently than we have thought. It is sometimes due to simple ulceration of the esophagus, but usually it is reflex, and as such may be associated with a great many conditions. It is the impression of the clinic that gastro-intestinal lesions, especially gastric and duodenal ulcers, are potent factors in its production. Underlying all of these factors is a definite neurotic state of the patient.

Spasmodic stenosis may occur at any level, but it is especially prone to occur in the cricoid region and at the level of the diaphragm.

In cases occurring in the cricoid region one is impressed with the increased resistance to the passage of the esophagoscope;

there is very little dilatation, the mucous membrane is perfectly normal in appearance, and if firm pressure is exerted the spasm relaxes and the tube passes on through the esophagus.

The most interesting cases are the cases occurring at the level of the diaphragm. These cases have been spoken of in the literature under the head of "cardiospasm," but this term really should not be used, as the condition is not one of spasm of the cardia, but one where the spasm occurs some distance above the cardia at the level of the diaphragm. Jackson uses the term "hiatal esophagismus" in describing this condition. The endoscopic picture depends mostly upon the duration of the condition. Most of the cases studied are those in which the condition has existed for a number of years. There is very marked dilatation of the esophagus above the seat of the trouble; the mucous membrane shows definite evidence of chronic inflammation and may show some areas of superficial ulceration. The dilatation is so great in some of the cases that it is necessary to wash out the esophagus before a satisfactory examination can be made. I recall one case in which more than a quart of thick mucous fluid was removed. In these cases if gentle but firm pressure is made the spasm relaxes and the esophagoscope passes into the stomach.

Ulceration.—Esophagoscopy is the only reliable means we have of diagnosing an ulcer in the esophagus, but to determine that it is a simple ulcer requires the exclusion of tuberculosis, lues, and malignant disease. Simple ulcer is usually associated with cicatricial or spastic stenosis. If stenosis is not present, we must think of the ulcer as probably being tuberculous, luetic, or malignant. The tuberculous ulcer is not associated with inflammatory changes in the mucous membrane, is not elevated, and does not bleed easily. The luetic ulcers are frequently associated with a great deal of scar tissue, with marked evidence of inflammation, with an elevated irregular border, and with very little bleeding when sponged. The malignant ulcers are characterized by being very red and angry looking, the surface is raised and irregular, bleeds very easily, and the base has a

very definite sense of resistance. Tuberculin and Wassermann tests should be done to aid in the differential diagnosis.

Diverticulum.—Esophagoscopy aids very much in the diagnosis of diverticulum, but the examination should always be preceded by a careful *x*-ray study so as to get a correct idea of the size and location of the pouch. Most of the cases occur high up, and the hernial sac is found to come off from the esophagus just below the cricoid cartilage; however, it may occur lower down, and is then due to adhesions from some of the surrounding organs to the esophagus, these causing traction and pouch-like dilatation. In doing esophagoscopy in these cases the tube apparently enters a blind pouch, but if careful examination of the anterior wall of the pouch is made a slit-like opening will be found which is the entrance to the lower portion of the esophagus. The finding of this opening makes the diagnosis complete and differentiates the condition from cicatricial stenosis with dilatation.

Pressure Stenosis.—In this condition the stenosis is usually due to an enlarged thyroid, mediastinal disease, aortic aneurysm, or enlarged heart. Each of these conditions is a contraindication to esophagoscopy, and the examination should not be resorted to unless it is for the removal of a foreign body.

Foreign Bodies.—In suspected cases of foreign body in the esophagus one should first have an *x*-ray study, and if by this method a foreign body is found, its size, shape, and location is to be carefully noted. If the foreign body is small and not very dense, it may not be located by the *x*-ray. In these cases it is necessary to search for the intruder endoscopically. If the foreign body is very large, it will be necessary to give a general anesthetic for extraction, as the relaxation produced by general anesthesia makes it possible to remove it with less traumatic injury to the esophagus and danger to the patient. As mentioned before, ether is the only anesthetic which can be used with safety. All of the mechanical problems connected with the removal should be worked out and necessary instruments at hand before an attempt at removal is made, as an unsuccessful attempt makes subsequent efforts more difficult. About

90 per cent. of foreign bodies that lodge in the esophagus are found above the cricoid cartilage, and these can usually be removed by the aid of the esophageal speculum. Those located in the middle and lower third of the esophagus require very careful endoscopic study and manipulation. If the foreign body has been in the esophagus a number of days the difficulty of extraction is increased by inflammatory swelling and edema; therefore the endoscopist should proceed very carefully so as not to override the foreign body and pass it unnoticed. When located, the foreign body should be studied and the best method of removal decided upon, and then the instrument best adapted to its extraction should be used. The after-care of the patient consists in giving of nothing but ice-cold liquids, or ice-cream for forty-eight hours, and then a bland, non-irritating diet until all the symptoms have subsided—no drugs are indicated. If the foreign body has caused ulceration the case should be watched for symptoms of stenosis which may occur when healing takes place.

TREATMENT

Spasmodic Stenosis.—In treatment of spasmodic stenosis one has to remove if possible the etiologic factors; for example, if the spasm is associated with gastric or duidenal ulcer, this condition must be treated. To control the spasm there is no drug that compares with belladonna. My custom has been to give the belladonna to the physiologic tolerance, sometimes giving as much as 40 to 50 drops three times a day. In all the cases of esophageal spasm that I have treated I have not found one that could not tolerate very large doses. I have also given these patients small doses of mineral oil three times a day to allay the irritation in the mucous membrane. After the patient is well under the influence of belladonna (usually by the tenth to fourteenth day) mechanical dilatation is begun. For the cases occurring in the upper third I have simply passed the large esophagoscope; this has relieved most of the cases after the first passage. In a few it has been necessary to repeat the treatment. The cases which have occurred at the level of the diaphragm have been treated with the Plummer dilator either

with air or water pressure. In cases where there was difficulty in getting the dilator in place the olive tip has been threaded over a thread swallowed the day before, and with the thread as a guide there has been no difficulty in placing the dilator and dilating the stricture. This treatment is repeated twice a week, and later, when the patient has improved, once a week. The other methods are mechanical divulsion from above and gastrostomy with forcible dilatation from below. The choice between using the mechanical divulsor or dilating with water pressure is a personal one, as both methods give good results, but I do not see anything to be gained in doing a gastrostomy with forcible dilatation from below when these cases can be dilated from above without operative treatment.

These patients should be kept on small quantities of liquid food every two hours while dilatations are being made. By feeding in this manner all pressure is removed from the esophagus. After the patient has been relieved clinically, soft food may be added—no coarse or irritating foods should be given until a few months after treatment has been discontinued. In cases with marked dilatation the esophagus should be emptied of all food before retiring, as this removes all irritation and relieves some of the annoying symptoms. While treating these cases we have made frequent fluoroscopic examinations, and while the patient has been relieved clinically the esophageal dilatation has persisted.

Cicatricial Stenosis.—In this condition there is an associated spasmodic condition as well as the organic lesion which calls for treatment. The associated spasm is treated by giving belladonna and mineral oil. The belladonna should be given to the point of physiologic tolerance. The management of the organic stenosis depends on the extent to which the lumen of the esophagus is narrowed. If the esophagoscopic examination shows that the stenosis is of moderate degree, that the mucous membrane above the stricture is not inflamed or ulcerated, the treatment consists of simply dilating with a bougie or a silk woven sound. In these cases the silk woven sound is to be preferred, as it is not necessary to dilate through the esoph-

agoscope. In cases of high-grade stenosis, where the patient is starving and the tissue suffering for want of fluid, the first thing to do is a gastrostomy, and by feeding in this manner the esophagus is given absolute rest and at the same time the patient is nourished. It is absolutely impossible to treat the esophageal condition unless the esophagus is given complete rest. When the patient's condition improves an *x*-ray study is made to locate the level of the stricture and to note the amount of dilatation above the stenosis; an esophagoscopic examination is also made to note the character of the stenosis and the amount of ulceration and inflammation above the obstruction. No dilatation should be attempted while there is ulceration and inflammation present. It has been my rule to give nothing by mouth except belladonna and mineral oil until after the esophagus has been dilated a number of times. In the beginning the olive-tipped bougie is passed through the esophagus and later on the silk woven bougie is passed without the 'scope. The gastrostomy opening should not be closed until the esophagus can be dilated to normal size. When mouth feeding is resumed the bland, non-irritating liquids are given, and if these are well tolerated the diet should be increased, avoiding, however, for a long time coarse vegetables and uncooked fruits. In cases where the stenosis is complete a gastrostomy must be done to prevent starvation, and an attempt should be made to relieve the stenosis by operation.

Ulceration.—All patients with ulceration of the esophagus should be placed on a bland, non-irritating diet, and frequently it is necessary to allow nothing but liquids. If the ulceration is associated with tuberculosis or malignancy the treatment is merely palliative. If due to lues, it responds to antiluetic treatment. If it is a simple ulcer it should be treated by the application of some of the silver salts—argyrol in a 20 to 25 per cent. solution being applied endoscopically every few days—usually three to four applications will suffice.

Carcinoma.—Unfortunately, the only treatment is palliative. When obstruction occurs, some advocate intubation of the esophagus; others favor dilating with sounds, but both of

these methods mechanically irritate the growth. I believe that it is better judgment not to disturb the esophagus, but to do a gastrostomy; this removes all irritation from the malignant growth and gives an opportunity to properly nourish the patient, adding materially to the comfort.

I have not discussed the treatment of diverticulum, as it is obviously surgical; nor pressure stenosis, for it is only amenable to treatment when the underlying cause can be removed.

CONCLUSIONS

First: That esophagoscopy can be done with very little discomfort to the patient.

Second: That esophagoscopy is a valuable aid in the differential diagnosis in diseases of the esophagus.

Third: That esophagoscopy is essential to the successful treatment of cicatricial and spasmodic stenosis and ulceration of the esophagus.

Fourth: That esophagoscopy is the only safe means for the removal of foreign bodies from the esophagus.

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THE ROENTGENOLOGIC SIGNS OF JOINT LESIONS IN CHILDREN

Differential Diagnosis by the *x*-ray Between Rickets, Syphilis, Scurvy, and the Condition Known as Perthés' Disease.

THE object of this clinic is an attempt to systematize and, if possible, arrange a classification of the various lesions of the joints of children from the changes that are seen upon an *x*-ray plate.

All clinical signs were disregarded, and the study was based entirely upon data obtained from the *x*-ray plate.

The first factor obtained seemed to show that there was a fairly definite relation between the age of the patient and the type of lesion seen. To one accustomed to studying *x*-ray plates and one familiar with the development of the bony structure age can be determined from the *x*-ray plate with a fair degree of accuracy.

Accordingly, we found that the vast majority of lesions could be arranged roughly into three age periods:

1. Those occurring from birth up to three or four years.
2. Those occurring from three or four years up to seven years.
3. Those occurring from seven years up to the adult age.

In the first class we found that from birth up to one year tuberculous infections were so infrequent that they could be practically disregarded. After one year, while tuberculous infections occur, we do not begin to see them with any degree of frequency until we reach the third or fourth years. In the same way, acute epiphysitis, while more frequent than tuberculosis, follows approximately the same course.

In this period we will find that the joint changes are very largely confined to the lesions arising from rickets, syphilis, and scurvy.

In the second age period we find that the three most common lesions of the first group have practically disappeared, to be replaced by the lesions of tuberculosis and acute non-tuberculous infections.

In the third age period we have the lesions of period No. 2 with one other added, namely, Perthés'.

It must be remembered that the age classification is only approximate, and frequently the periods may overlap.

Now let us consider the changes that take place with the lesions in age period No. 1. Taking them up in the order of their frequency, we will first discuss rickets.

We will first consider the changes that take place in the joints, and second, the remote or constitutional changes. We find that there is multiple joint involvement. There is fluid and swelling of the peri-articular tissues. The cartilaginous surfaces of the joint are intact, but there is a marked disturbance of the epiphyseal line. We find that the epiphysis becomes softened and has a tendency to spread out. There is slight condensation at the epiphyseal line and the end of the bone has an inverted saucer-shape appearance (Figs. 285, 286). The epiphysis proper is never disturbed and the changes are confined entirely to the epiphyseal line. This saucer-shape expansion is most marked in the weight-bearing joints. The most typical joints for diagnosis are the lower ends of the tibia and radius.

Now since these joints are swollen and sometimes painful, there is limitation of motion, and, consequently, we get a general atrophy of the bones, not only due to disuse but also due to the fact that the disease is a nutritional one. When the attack is especially severe and of long standing the atrophy becomes so extreme that the bones lose almost all their structure and are so seriously weakened that the slightest trauma will produce fractures. In the severe cases multiple fractures are quite common.

The writer has seen one case in which there were eighteen

fractures of the long bones, one bone, namely, the femur, having four distinct fractures. On account of the extreme atrophy we do not, as a rule, have periostitis, though occasionally it may be present to a slight degree.

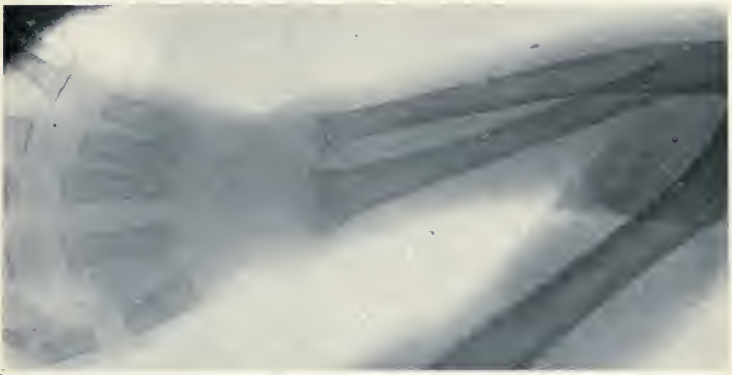

Fig. 286.

Fig. 285.

Figs. 285, 286.—Rickets: Shows the periarticular swelling and the inverted saucer-shape appearance of the epiphyseal line, with bone condensation.

Care must be taken not to mistake this condition for osteogenesis imperfecta. In this disease we have the marked atrophy and the multiple fractures, but the point of differential diagnosis rests upon the fact that there are no joint and epiphyseal changes.

In the rachitic conditions it is always well to examine the chest, as we will find in typical cases the rosary at the ends of the ribs, due to the same saucer-shape expansion of the epiphyseal line of the ribs. Here again we get a secondary change in the lungs. We have spoken of the softening of the bones, due to the absorption of the calcium salts in the epiphyses. These two changes have weakened the costochondral region so very materially that, with the negative pressure in the chest coupled with the muscular pull of respiration, the costochondral region bends and is pulled in upon the lungs sometimes to such an extent as to affect the proper aëration of the lungs. We frequently find a band of consolidated lung just beneath the costochondral articulation which runs parallel to the sternum on each side. This consolidation is, in reality, an atelectatic strip from pressure, and is generally fatal.

With proper treatment the epiphyseal changes clear up and there is frequently left behind a line of slightly condensed lime salts running across the bone, due to faulty calcification. The writer has on numerous occasions seen four or five such parallel lines, indicating that there had been that number of acute exacerbations in the course of the disease. When deformities have occurred such as those described in the bony structure of the chest or in bowing of the long bones, they, of course, invariably persist.

It is well to mention that pulmonary complications are extremely common in rickets, due to the marked disturbance of the proper aëration of the lungs from costochondral pressure.

To summarize the chief points:

1. Occurs in the very young, especially first two years.
2. Joint itself intact, spreading out of the epiphyseal line.
3. Atrophy, with the frequent occurrence of fractures.
4. Periostitis generally absent, though occasionally present.
5. Marked pulmonary changes.
6. No subperiosteal hemorrhages.

In syphilitic lesions, just as in rickets, we have the joint and bone changes. The joints are generally multiple; there is sometimes periarticular swelling and fluid in the joint. The

cartilaginous surfaces of the joint are intact, but, like rickets, there are marked disturbances in the epiphyseal line region. Here the changes take place upon the diaphyseal side of the line. There is, however, no softening or saucer-like expansion of the epiphysis. There are localized areas of softening and destruction of the bone just beneath the periosteum, at the point

Fig. 287.—Syphilis: Shows partial destruction of the epiphyseal line and the bone beneath it. Marked periostitis.

where the cartilage of the joint begins. These destroyed areas are circumscribed and suggest that they had been bitten out by a Rongeur forceps (Figs. 287, 288). They start at the epiphyseal line and extend back into the bone proper. The epiphyses in the undestroyed portions will be perfectly normal. Atrophy is generally absent, so we seldom have multiple fractures. Syphilitic infections always produce bone, so that we practically

always have more or less new periosteal bone. The chest and lungs are never involved. To summarize the chief points:

1. Occurs in the very young, especially in the first two years.
2. Joint itself intact, no spreading out of the epiphyseal line, but gouged out areas in the diaphysis.

Fig. 288.—Syphilis: Shows the gouged out area in the lower end of the humerus and slight periostitis.

3. No atrophy, and we seldom have fractures.
4. Periostitis almost always present and generally excessive.
5. No pulmonary changes.
6. No subperiosteal hemorrhages.

Since rickets and syphilis are seen so frequently in the lower walks of life, these two conditions are frequently associated in

the same individual, and it is often difficult to determine from an *x*-ray standpoint which is the predominating factor in the case.

In scorbutic lesions, just as in syphilis and rickets, we have joint and bone changes. The joints are generally multiple, there is occasionally periarticular swelling and fluid in the joint.

Fig. 289.—Scurvy: Shows a huge organizing hematoma with definite calcium border, and the Trümmer zone just behind the epiphyseal line of the femur, and also beneath the epiphyseal lines of the tibia and fibula.

The cartilaginous surfaces of the joint are intact, but, like rickets and syphilis, there are marked disturbances in connection with the epiphyseal line. All the changes take place upon the diaphyseal side of the epiphyseal line. The epiphysis and epiphyseal line are intact, no changes taking place at all at these two places. There is no saucer-shape expansion of the end of the bone as in

rickets, or localized areas of softening and destruction as in syphilis. Just back of the epiphyseal line, from $\frac{1}{2}$ to $\frac{1}{4}$ inch, is what apparently is a second epiphyseal line, which, in reality, is a band of localized destruction about $\frac{1}{16}$ inch in diameter, extending through the entire bone and parallel to the epiphysis. The edges of this band are frequently denser than the normal bone, and gives the appearance of eburnated bone, being due probably to the condensation of calcium salts (Fig. 289). This band (Trümmer zone) gives the appearance as if a surgeon had operated and taken out a cross-section of the bone.

Atrophy is sometimes present, but, on account of the periosteal bone, fractures are infrequent. In this condition we have frequent hemorrhages beneath the periosteum which elevate the periosteum, and later there is organization of the hemorrhage (Fig. 290). The organization produces such a hard tumor that the writer has seen 2 cases of this condition that were mistaken for sarcoma, especially after the acute scorbutic symptoms had subsided. The *x*-ray picture, however, is so definite that, once seen, a mistake in diagnosis will rarely be made.

To summarize the chief points:

1. Occurs in the very young, generally in the first and second years.
2. Joint itself intact. Epiphysis and epiphyseal line not disturbed, but the formation of this destructive zone behind the epiphysis.
3. Atrophy occasionally present, but seldom fractures.
4. Periostitis practically always present.
5. No pulmonary changes.
6. Subperiosteal hemorrhages frequently present.

It will be noted in these three conditions—namely, rickets, syphilis, and scurvy—that they all occur at approximately the same age period and that the joint surfaces are intact. The differential points in diagnosis depend upon the changes in and around the epiphyseal line and the character of the periosteal changes.

In rickets the changes are confined to the epiphyseal line; in syphilis the epiphyseal line and bone directly behind it are in-

volved; while in scurvy the epiphyseal line is intact and all the changes take place in the bone just behind it. In rickets there

Fig 290.—Scurvy: Shows a small hematoma and Trümmer zone at the lower end of the femur and the head of the tibia.

is seldom periostitis; in syphilis there is marked periostitis; while in scurvy the periostitis is frequently accompanied by subperiosteal hemorrhages.

As we come to the close of this age period tuberculosis and acute epiphysitis of the joints become more frequent, and practically supplant rickets, syphilis, and scurvy in the second age period.

In tuberculosis we find that the lesion is generally confined to one joint. There is periarticular swelling and fluid, but on account of the periarticular involvement the joint becomes very hazy and indistinct in the first stages of the disease. As the lesion progresses we begin to find that the articulating surfaces of the joint become irregular and worm-eaten and the bones forming the joint become very atrophic from disuse. The disease slowly destroys the cartilage and the bone beneath, but never metastasizes in the head of the bone, but proceeds by direct extension. As the disease subsides there is frequently subluxation, and when ankylosis takes place it is largely fibrous, there being but little bone production.

In acute epiphysitis, non-tuberculous, it is frequently impossible to differentiate it from tuberculosis, except that, as a rule, the joint does not become as hazy and indistinct. The lesion is generally confined to one joint and the destruction is more rapid and the direct extension is more irregular. There appear frequently focal spots of disease in the bone not directly connected with the primary infection of the joint. As the disease subsides there is marked production of new bone, and the ankylosis is practically always bony in character.

It will be noted that in the early acute stages of these two lesions it is frequently impossible to make a differential diagnosis, but when the stage of repair has been reached the marked production of new bone will indicate that the infection was pyogenic and not tuberculous.

In this age period and the succeeding one we will occasionally see joints in which there is swelling and fluid. Repeated examinations at intervals will show that this type of joint is returning to normal. These must be looked upon as merely a synovitis produced probably by trauma, so slight as not to have been noticed.

At the end of this second period and also part of the third

period we occasionally see that uncommon condition first described by Perthés. In Perthés' original communication he described this lesion, and all of his cases were limited to the hip-joint. In the writer's series of cases they were also confined to the hip-joint, and if they do occur in other joints, so far they have not been recognized.

Fig. 291.—Perthé's disease: Shows the flattened, eburnated epiphyseal head with a small fragment broken off.

This condition is of peculiar interest in that all the signs and symptoms point to a tuberculous infection, but does not react to tuberculin, and recovery is much more rapid and the joint returns more nearly to normal. The *x*-ray picture when once seen is very typical. There is no hazing and clouding of the joint, the epiphysis is crushed down somewhat and flattened, and there is marked eburnation of the bone beneath the car-

tilage, due to the packing down of the calcium salts, and occasionally small fragments may be broken off (Fig. 291). The lesion may be unliteral or bilateral. The changes are entirely confined to the head of the femur, the acetabular surfaces apparently never being involved.

With the union of the epiphyses we reach adult life, and then comes that great arthritic group, namely, infectious, atrophic, and hypertrophic arthritis. This group will not be discussed since it is not in the province of this clinic.

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INTRODUCTORY REMARKS TO A DISCUSSION OF DIABETES

BEFORE commenting upon the cases of diabetes I have shown you I propose to review briefly the fundamental facts of carbohydrate metabolism. Every step in the treatment of diabetes and all of our clinical knowledge of the disease rests upon these facts. If you are familiar with them, then you know all there is to be known about diabetes; if you ignore them, you will never adequately appreciate the clinical problems this disease presents. Let us then look upon the condition from this standpoint before we say a word about treatment.

Sugar is furnished the body mainly in the form of starch, cane-sugar, and milk-sugar. These polysaccharids are split into the simple hexoses—glucose, levulose, galactose. If absorption proceeds slowly, these sugars are converted in the liver into glycogen; if absorption is too rapid, a portion may appear in the urine. Normally, mellituria never occurs upon a starch diet, but following large amounts of the simple hexoses or of cane-sugar and milk-sugar, glucose, levulose, or galactose may appear in the urine, and under exceptional conditions small amounts of unconverted cane- or milk-sugar. While glycogen is readily formed from any of the three hexoses, when it breaks down it always yields glucose. In the blood there is a relatively constant level of glucose concentration, averaging about 0.08 per cent. The normal limits vary from 0.07 to 0.12 per cent. When this normal high level is appreciably exceeded sugar appears in the urine. All glycosurias except the glycosuria following phloridzin administration and certain instances of so-

called renal diabetes are consequent upon hyperglycemia, but the kidneys do not play an entirely passive rôle. Aside from instances of gross renal disease with impaired function, the permeability of the kidneys for glucose varies in different individuals and in the same individual at different times. However, the range of renal adaptability is relatively small. This constant blood-sugar level is maintained by a mechanism of great complexity which we are only beginning to understand. From the blood glucose is taken by the cells and utilized in the manufacture of complex substances forming an integral part of their structure, or stored as glycogen, or directly burned. As an integral constituent of cell substance glucose and its derivatives play an insignificant part in the animal economy as compared with their important rôle in plants. In the latter they are the chief constituents of the supporting and protecting tissues, whereas in the former these structures are protein in composition. Next to the liver, the muscles possess the main glycogen reserve of the body. Many other, indeed, perhaps all, cells possess slight glycogenic power. The burning of sugar is not a direct combustion. The decomposition to water and carbon dioxid is a slow progression through many complex chemical stages, the intricate nature of which has not yet been fully elucidated. If the supply of carbohydrate is abundant and all of the energy needs of the body are thereby covered and the glycogen reserve is complete, sugar may be further stored as fat. The weight of evidence points to the connective tissues as the seat where this conversion takes place. No matter what means we employ to reduce it, the glucose content of the blood is maintained desperately at its constant level. In starving animals it is reduced but little below the normal. If carbohydrate ingestion be greatly reduced or entirely suppressed, the animal organism will grasp its glycogen reserve, and, when this is exhausted, manufacture sugar from protein.

This brief statement of the essential and generally accepted facts of carbohydrate metabolism is offered merely as a loose framework upon which to hang more interesting details of the story.

When carbohydrates are taken by mouth, if absorption proceeds slowly an unlimited amount can be utilized. In normal animals it is impossible to produce mellituria by feeding excessive amounts of starch. Even when disaccharids or monosaccharids are administered in conjunction with other food, sugar seldom appears in the urine. However, when sugar is taken into the fasting stomach, absorption procceeds with remarkable rapidity, and if large amounts are taken, sugar flows off in the urine. There is a wide individual variation in tolerance for sugar, but, on an average, 120 grams of glucose may be taken without producing mellituria. This "assimilation limit" for sugar is influenced by a great variety of conditions, and the interpretation of changes in the level is surrounded with difficulty, but its estimation is the first and a very important step in all clinical studies of carbohydrate metabolism.

This digestive factor in glycosuria is of practical importance. In all probability upon it depends the difference in the utilization of different starches. For instance, it is found in cases of severe diabetes that there is often distinct improvement in the assimilation of sugar when large amounts of certain carbohydrates are administered. Such improvement frequently follows an oatmeal cure. Evidence favors the view that the benefit of oatmeal depends largely upon the difficulty of digestion and the slowness of absorption.

If sugar absorption be sufficiently slow, nearly all of the sugar reaches the liver and there is built up into glycogen. When sugar in large amounts is given, but still below the assimilation level, glycogen formation often proceeds with such rapidity that the sugar content of the blood in the general circulation is temporarily reduced. It is possible that a small amount of sugar goes directly into the general circulation either through a failure of the liver to retain it all or, more probably, by way of the thoracic duct.

In well-nourished individuals with a satisfactory glycogen reserve all of the ingested carbohydrate is not converted into glycogen; some is burned directly and some is converted into fat.

A more accurate way to test carbohydrate assimilation than

by the alimentary route is to avoid the influence of digestion and absorption by injecting the sugar subcutaneously or directly into the blood-stream. Blumenthal found that rabbits became glycosuric following the intravenous injection of 1 gram of glucose per kilogram of weight, and that less sugar was needed for the purpose with dilute than with stronger solutions. After giving an amount just short of the assimilation limit, a second injection of even a very small amount promptly caused glycosuria. The prompt removal of a definite sudden increase in the blood-sugar Blumenthal calls the saturation limit, in contradistinction to the utilization limit which designates the utilization of a constant though moderate excess. The utilization limit he determines by injecting small amounts at frequent intervals. The saturation limit for glucose and levulose Blumenthal finds about equal; for galactose much lower, and for saccharose and lactose very low. Biedl and Kraus have injected from 200 to 300 c.c. of a 10 per cent. glucose solution in man without producing glycosuria or polyuria. Woodyat and his co-workers have amplified Blumenthal's observations in a striking way. They have devised an instrument that will deliver a constant stream into the vein, and they find the utilization limit for glucose in a normal person to average 0.85 gram per kilogram per hour.

Of the disaccharids, maltose alone is utilized when injected directly into the blood. Saccharose and lactose are excreted almost quantitatively. It has been claimed that if these sugars are repeatedly injected, ferments gradually accumulate in the blood which split the disaccharids, and the resulting monosaccharids are then utilized. However, this claim has not been substantiated. As would be supposed from the galactose content of milk-sugar, saccharose is more readily utilized than lactose.

By the subcutaneous method of testing the utilization limit for sugar, larger amounts are tolerated than intravenously. By this method it is found that galactose is less readily utilized than glucose or levulose, but in contradistinction to the results of the intravenous method glucose is much more readily utilized than levulose.

As Allen has insisted, there is, strictly speaking, no true limit of tolerance for glucose. If the assimilation limit were real, then if a small amount of sugar were excreted after administering 150 grams of glucose, 50 grams should be eliminated after the ingestion of 200 grams of glucose. However, this is not the case, for no matter how much glucose above the tolerance limit is administered, but a small amount of the excess appears in the urine. Von Noorden gives the following data:

Amount of glucose.	Healthy individual A excretes.	Healthy individual B excretes.
100 grams		
150 "	0.15 gram.	
180 "	0.25 "	0.23 gram.
200 "	0.26 "	0.71 "
250 "	0.52 "	0.64 "

Worm-Miller has these figures:

After	50 grams of saccharose,	0.1	gram of sugar appeared in the urine.					
After	100 " "	0.85	"	"	"	"	"	
After	250 " "	1.8	"	"	"	"	"	

Sugar introduced into the body parenterally is partly built up into glycogen, partly burned, and partly converted into fat. The body cells apart from the liver have a marvelous capacity for managing glucose. In frogs, extirpation of the liver does not reduce the tolerance for glucose. In geese, cutting off the portal circulation reduces but little the tolerance for glucose, but the levulose tolerance is considerably reduced. In dogs with Eck fistula the tolerance for glucose is unaltered, for levulose but little reduced, while galactose is excreted almost quantitatively. In rabbits, phosphorus-poisoning reduces the tolerance for levulose and for galactose, but not for glucose. Worner concludes from his studies that the tolerance for galactose runs parallel with the liver damage.

In considering the relation of the liver to glycogen, it is useful to distinguish three functions: (1) The formation of glycogen from sugar—glycogenesis; (2) the breaking down of glycogen into glucose—glycogenolysis; (3) the formation of gly-

cogen from substances other than carbohydrates—glyconeogenesis.

Glycogenesis: Under normal conditions the liver manufactures glycogen from the sugars that reach it through the portal circulation. Under carbohydrate feeding its store of glycogen may reach fully 15 per cent. of the total weight. The exact mechanism of glycogen formation is not understood. There is a very definite enzyme in the liver and in other tissues of the body and in body fluids that splits glycogen into glucose. Since the reversible action of enzymes is a common biologic phenomenon, it has been assumed that glycogenase may build up as well as break down glycogen. Cremer thought he obtained evidence of glycogen formation by mixing yeast juice and glucose, but his results have not been confirmed. Indeed, innumerable attempts to produce glycogenesis with glycogenase and other ferments have failed. It has been suggested that sugar undergoes some chemical change either by enzyme or hormone action before being condensed to glycogen, but the evidence is inconclusive. Nor is there conclusive evidence from which to decide whether this function is stimulated directly or is under the influence of nervous control. The technical difficulties of perfusion experiments render the results questionable. The fact that adrenalin while producing hyperglycemia and glycosuria, still, at the same time, causes an accumulation of glycogen, suggests that at least some nervous control is exercised.

It has been thought that glycogen is not produced from the different sugars in exactly the same way. In dogs with pancreatic diabetes, Minkowski found that there was a storing of glycogen and an improved carbohydrate metabolism after levulose, while no glycogen formation followed glucose administration. Von Noorden is convinced that similar conditions obtain in man, and upon this authority the difference has been made much of in the treatment of diabetes. Some years ago Magnus-Levy expressed the conviction that in severe cases of diabetes there was no apparent difference in the behavior of the two sugars, and recently Minkowski's experimental work has not been confirmed.

Glycogenolysis, as has been stated, is directly produced by the enzyme glycogenase. This enyzme is found in the liver and in all the body tissues and juices. Whether it is formed in the tissues or appropriated by them from the body juices is undetermined. It would appear that mainly the pancreas furnishes the blood and lymph with glycogenase. All attempts to identify variations in glycogenase as responsible for abnormalities in carbohydrate metabolism have failed. MacLeod has shown that glycogenolysis caused by stimulation of the splanchnic nerves proceeds without change in the amount of glycogenase. Further studies led him to conclude that the process depends upon the reaction in which the enzyme works, its activity being greatly increased in a slightly acid environment. Glycogenolysis proceeds with great rapidity when the liver is removed from the body and after death. However, under normal conditions it is largely under nervous control, and this mechanism involving the reciprocal and antagonistic activities of the various endocrine glands is one of the most fascinating chapters in recent medical discoveries.

Glyconeogenesis is intimately bound up with glycogenolysis. Whenever the body demands a fresh supply of sugar the glycogen reserve of the liver is called upon. The muscles and probably other tissues hold their glycogen more tenaciously. As the glycogen reserve in the liver is diminished, a fresh supply is built up from the carbohydrates of the food, and if these are not available, sugar is formed from protein and perhaps from fat. Under all conditions, even in extreme starvation, the body fights to keep its blood-sugar at a constant level. This effort is apparently as fundamental and far reaching as the attempts to maintain a constant reaction and salt equilibrium. Pflüger was the powerful opponent who held out so long against admitting the formation of sugar from protein, but shortly before his death he realized the absolute necessity of its recognition and added valuable evidence to its support. Study upon patients with diabetes and upon diabetic animals has shown that the amount of sugar produced cannot be accounted for by the glycogen reserve of the body and the carbohydrate ingested.

During starvation and when fed solely upon protein completely diabetic animals manufacture sugar from protein in a constant proportion. If all of the carbon in protein were converted into sugar, then for each gram of nitrogen 8 grams of sugar would be formed. It is remarkable that in pancreatic diabetes in dogs during starvation or upon a wholly protein diet the nitrogen-dextrose relation is constantly in the neighborhood of 2.8; in phloridzin diabetes under similar conditions it is 3.6; when pancreas and thyroid are both removed, it is said also to equal 3.6. Lusk has accepted 3.6 as the maximum sugar formation from protein. It has been objected to these figures that in estimating the urine nitrogen no account is taken of the endogenous or cellular nitrogen metabolism. It is assumed that all protein is converted into sugar. Corrected in accordance with these views, the dextrose-nitrogen ratio in pancreëctomized dogs is 3.3; in phloridzin and severe human diabetes, 6. Gigon regards 6 as the maximum figure and refuses to recognize higher values that have been reported in man by Falta and others.

Not all portions of the protein molecule furnish sugar with equal facility. Although it would seen reasomable to select glucosamin as the readiest source of sugar, all investigations with this derivative indicate that it is not utilizable in this manner. The work of Embden and of Lusk has shown that certain of the amino-acids, for instance, glycocoll, alanin, aspartic acid, and glutamic acid, readily form sugar, while others, for instance, leucin and tyrosin, do not. Apparently, those amino-acids that fail to yield sugar are easily changed into the acetone bodies. All of the carbon atoms of glycocoll and alanin are directly convertible into sugar, while but three of the four carbon atoms of aspartic acid and three of the five of glutamic acid are susceptible of such transformation. The experiments of Embden make it altogether probable that at least the main stage in the conversion of the amino-acids into glucose takes place in the liver.

It is a matter of great practical importance to know if all proteins are equally sugar yielding. Such information might

point valuable lessons in the treatment of diabetes. It has been found that of all proteins, casein yields sugar most readily. This has been explained by the ease and rapidity with which casein is split in the intestinal canal, the body being thus flooded with amino-acids. This is a reasonable explanation and is supported by analogy with carbohydrate utilization, slow digestion and absorption facilitating its conversion into glycogen. Rolly and Oppermann find in diabetes that meat and aleuronat, a vegetable protein, affect the glycemia and glycosuria equally, except that when the latter substance is administered, the rise in sugar occurs later and endures longer. They ascribe the difference to the delayed digestion and absorption of the vegetable protein.

Estimating the amount of sugar that might come from carbohydrates and proteins, certain authors find in severe diabetes an excess which they conclude must come from fat. Feeding experiments have proved conclusively that glycerin is convertible into sugar, but even allowing for this constituent of fat there is still a deficit which they believe is derived from the fatty acids. The question is still unsettled and has given rise to a lively controversy.

It is needless to comment upon the important place the liver occupies in carbohydrate metabolism. However, the present attitude is to regard it as a passive organ yielding its supply of sugar and manufacturing fresh material under the pressure of outside influences. With the exception of phloridzin and pancreatic diabetes all other clinical and experimental forms of glycosuria depend in large measures upon the glycogen content of the liver. Even in phloridzin and pancreatic diabetes since the liver is the only, or at all events the principal, site of glyconeogenesis, glycosuria depends upon its integrity. Pflüger justly says without the liver there can be no diabetes. In frogs if the liver be removed, extirpation of the pancreas causes no glycosuria. Hedon finds that pancreas extract injected into the portal circulation of dogs with pancreatic diabetes has a striking effect upon the glycosuria, whereas, injected into the general circulation, it has no influence. If these results are

confirmed, they would indicate that the liver in some way activates the pancreatic secretion.

Glycogenesis is such a fundamental function of the liver that its exercise is continued under the most adverse conditions. In starving animals, the liver builds glycogen up to the time of death, and even in severe diabetes the property is not totally lost. It is probable, then, that this function would be seriously impaired only in extreme hepatic disease. Clinical evidence supports this view. Cirrhotic and parenchymatous lesions are frequently found in the livers of diabetics, but all investigators agree in regarding them as secondary to and not the cause of the disease. The striking increase in Kupffer cells reported by Fisher and the nuclear distribution of glycogen noted by Huebschmann are interesting pathologic findings, but have no casual relation to the disease. There has been a lively controversy between clinicians as to the existence of purely hepatic diabetes. French authors continue to describe such cases, but the condition has neither firm clinical nor experimental evidence for its support, and the majority of clinicians refuse to recognize it.

Since the discovery of the glycogenic function of the liver by Claude Bernard, sugar tolerance has been used as a test of hepatic function. The French school has claimed great clinical value for the test, while German authors have with equal firmness rejected it as useless. Straus in 1898 thought he had discovered the reason for this discrepancy. The French clinicians had been using 150 grams of cane-sugar; the Germans, 100 grams of glucose, in performing the test. Straus found that these sugars are not utilized with equal facility, and attributed the difference to the levulose in cane-sugar. He, therefore, devised a test of liver function, using levulose as a test-meal. The sum of clinical investigation shows some relation between liver injury and levulose assimilation, but authors disagree widely in their opinion of the clinical value of the test. Churchman, after a study of cases in the wards at the Johns Hopkins Hospital, concludes the test has little clinical value. Since experimental results indicate that galactose is handled exclusively

by the liver, Bauer proposed substituting galactose for levulose in testing liver function, and claims this change gives far better results. Bloomfield and Hurwitz give a good account of the difficulties surrounding the interpretation of these tests.

In the past few years interest in abnormal carbohydrate metabolism has been transferred largely from glycosuria to a study of the behavior of the sugar in the blood. Simplified methods of determining blood-sugar have facilitated clinical studies. In normal animals and in man it is found that the sugar content of the blood varies somewhat in different parts of the circulation. Lepine finds a higher content in the carotid artery than in the right auricle. Slight muscular exercise may increase, severe exertion reduces it. There is a well-marked rise after bleeding. Fever increases it. Various pathologic conditions, as nephritis, disease of the liver and intestines, anemia, and so on, influence it. It is increased by dyspnea, asphyxia, narcosis, and emotional conditions. Of special interest, however, is the relation of blood-sugar to carbohydrate digestion. It has long been known that alimentary glycosuria is often the earliest manifestation of beginning diabetes, and the behavior of the blood-sugar following carbohydrate ingestion, therefore, acquires special significance. In animals and in man the ingestion of sugar following a short period of starvation is followed after fifteen minutes by a definite rise in the blood-sugar; after one hour the amount is almost doubled; the hyperglycemia then gradually subsides and disappears at the end of three hours. In well-fed animals the rise is slower and less marked, and if tests be made in quick succession, each repetition is followed by a less decided change, until the effect is lost completely. Starch and certain vegetables have the same effect as glucose when administered upon an empty stomach, but the effect is diminished in proportion to the admixture of other foods. In man, bread eaten with butter has a much less decided influence upon the blood-sugar than bread alone. The digestive factor in carbohydrate metabolism has been pointed out. These studies in digestion hyperglycemia give us valuable

clinical hints for dietetic management of diabetes. Protein digestion has no influence upon the blood-sugar.

The condition in which sugar exists in the blood has given rise to much speculation. Reduction tests give larger amounts than polarization. The difference may be explained by the small amounts of levulose, maltose, pentose, and glycuronic acid that are sometimes present. All of these reducing bodies normally found in blood are grouped by Lepine as "sucre immediat." If blood be mixed with acid and heated and the sugar then estimated by reduction, a larger amount is found than before. This bound sugar Lepine calls "sugar virtuel." There is at present no value attached to these differences, and when blood-sugar is spoken of the "sucre immediat" is meant.

Since the blood-sugar dialyses in a normal way, it has been assumed that it exists free in the blood. On the other hand, many authors insist upon speculative grounds that the assumption of some form of loose combination is necessary to fit facts satisfactorily into any reasonable plan of sugar metabolism. Allen is the latest and most forceful of these advocates. He assumes that sugar before entering into the blood-stream combines with another substance, the resulting body having colloidal properties. This combining substance he calls, in terms of the well-known immunologic nomenclature, amboceptor. He assumes that the pancreas is directly responsible for the presence of this amboceptor, the absence of which is the cause of pancreatic diabetes.

Regulation of the sugar content of the blood is a fundamental property of the body. The regulating mechanism that guards against an excess of sugar resides partly in the tissues themselves. The early fall of postprandial hyperglycemia may be due in part to absorption of water from the tissues, for the hemoglobin often falls as the sugar proportion decreases. At the same time the tissues become saturated with sugar. However, a more important part of the regulatory mechanism resides in the kidney. When hyperglycemia reaches a certain level, sugar flows off in the urine. In this sense the kidneys may be likened to the overflow pipe of a cistern, but the compari-

son is only superficial, for their action is by no means passive. Under normal conditions glycosuria and hyperglycemia run fairly parallel. However, in diabetes there is by no means such a constant relation, for the relation varies in different individuals and in the same individual at different times. There is often marked glycosuria when the hyperglycemia is below the level frequently exceeded in normal individuals without loss of sugar in the urine. Indeed, in some severe cases of diabetes the blood-sugar is surprisingly low. In diabetic coma there is frequently an abrupt diminution in the urine sugar, while the blood-sugar ascends to a very high level. As is well known renal disease seriously affects the organ's permeability for glucose. In diabetes, when nephritis develops, glycosuria may entirely disappear, while the blood-sugar proportion increases. Experimental nephritis following injection of the salts of uranium and chromium frequently is associated with increased permeability and glycosuria. Luthje reports a patient developing glycosuria with the onset of a renal lesion. MacLeod has shown that the rate of blood flow in the kidney has a decided influence on sugar excretion. Such considerations make apparent the clinical value of blood-sugar determinations. These may prove to be not only our safest guide to the early diagnosis of diabetes mellitus, but likewise our most reliable source of prognostic and therapeutic information throughout the course of the disease.

Although the kidneys do not play an entirely passive rôle in glycosuria, still, with few exceptions, glycosuria is always secondary to hyperglycemia. The exceptions are the galactosuria of pregnant women, certain cases of so-called renal diabetes, and phloridzin diabetes. Experimentally phloridzin diabetes is the only true renal glycosuria. In starvation and upon a protein diet sugar is excreted in a constant proportion, the nitrogen-dextrose ratio being 3.6. Not only is there no hyperglycemia, but the blood-sugar is greatly reduced. The glycosuria in no way depends upon the glycogen content of the liver, for it occurs with equal intensity during inanition. It increases the glycosuria in animals with pancreatic diabetes, and such animals almost at the point of death and free from

glycosuria on account of advanced weakness again eliminate sugar from phloridzin influence. In severe phosphorus-poisonings it still causes glycosuria. Temperature and muscular exertion have no influence upon its action.

In man rare cases of glycosuria are distinguished by an absence of any relation between carbohydrate ingestion and sugar elimination, by an absence of hyperglycemia, and by their failure to develop under prolonged observation any of the usual symptoms of diabetes mellitus. Such cases have all the characters of a true renal glycosuria, although some experienced observers refuse to recognize renal diabetes as a clinical entity. There is good evidence for considering the galactosuria of nursing women a pure renal mellituria.

Of all the regulators of carbohydrate metabolism, the pancreas has held and still holds the point of highest importance. Removal of the organ in animals causes a severe glycosuria which persists whether sugar be given or withheld. In starvation or on a protein diet sugar is excreted in a constant proportion, the dextrose-nitrogen ratio being 2.8. The animal rapidly emaciates, acetone bodies appear in the blood, and death occurs in from two to four weeks. Besides the failure to utilize sugar there is also a profound change in the general metabolism. The hunger protein metabolism is increased threefold and fat consumption is likewise increased. This remarkable influence that the pancreas exercises upon carbohydrate metabolism is due to some substance secreted in the blood-stream, for the pancreatic duct may be tied off or transplanted so that the secretions are poured upon the surface of the body and no change in sugar metabolism occurs. When a small piece of the pancreas with the blood-supply intact is transplanted subcutaneously, glycosuria does not occur; when the graft is subsequently excised, diabetes promptly sets in.

Of still greater clinical interest than total extirpation of the pancreas are the results of partial removal. These experiments were first performed by Sandmeyer, and the condition has since been known as Sandmeyer's diabetes. When small portions of the pancreas are allowed to remain and the ducts are

tied, the animals at first do not become diabetic, but as the remaining portion of gland degenerates, glycosuria develops, and finally the picture following complete removal of the organ supervenes. Allen has shown that when a small portion of the pancreas is allowed to remain in communication with a patent duct, a balance is often struck, so that the animals are glycosuric after carbohydrate ingestion, but the urine remains sugar free on a protein and fat diet. In dogs and cats he has made the remarkable observation that the ultimate outcome of this mild diabetes may be completely controlled through the diet. If, on the one hand, animals are liberally fed with carbohydrate, the diabetic condition progressively increases, so that later they excrete sugar when given only protein food, and finally they emaciate and die a typical picture of fatal diabetes. If, on the other hand, the animals are fed upon a protein and fat diet, they are maintained in good condition, and not only is fatal diabetes avoided, but, indeed, after a certain period it is found that their tolerance for carbohydrate has increased. The practical importance of these observations needs no emphasis. It is the first solid experimental evidence to support the methods of treatment that clinical observation has already established.

It has long been assumed that the action of the pancreas upon carbohydrate metabolism is due to an internal secretion. There is much presumptive evidence in favor of this view. Transplantation and partial extirpation experiments can scarcely be explained upon any other assumption. However, it must be admitted that so far satisfactory evidence of the presence of an internal secretion has not been submitted. On three occasions we have thought that such evidence had been obtained, but in each instance disappointment quickly followed. Lepine in 1890 discovered that the disappearance of sugar from drawn blood was due to a glycolytic ferment which was bound to the leukocytes. Further experiments led him to believe that the ferment was greatly diminished in diabetes. Subsequent observations have disproved Lepine's impressions, and it has been pointed out that the glycolytic ferment in blood is too small in amount to adequately explain the normal combustion of sugar.

Cohnheim in 1903 found that whereas fresh extract of pancreas or muscle juice has little effect in destroying sugar, the two combined have marked glycolytic power. The simplicity and far-reaching importance of this discovery gave it wide acclaim. The studies of Claus and Embden and of Simpson have proved the results to be fallacious. Knowlton and Starling in 1912 found that the heart from a normal animal perfused outside of the body consumed more sugar than did the heart from a diabetic animal, and that the power of the isolated diabetic heart to consume sugar was improved by the addition of pancreatic extract to the perfusion fluid. In a series of convincing experiments MacLeod and Pearce failed to confirm these results. Starling has subsequently pointed out the source of error in his first experiments. However, the same question has been raised again by the work of Admont Clark. Clarke has shown that the utilization of sugar by the perfused living heart is greatly increased if the perfusion solution is first passed through the pancreas. The pancreas seems to supply something to Locke's solution circulating through its arteries which in some way brings about a better utilization of sugar. This pancreatic substance possesses some of the properties of an enzyme.

A conclusive proof of an internal secretion from the pancreas has been sought in the influence of normal blood which presumably contains this secretion and of pancreas extracts upon diabetes. The results of experiments undertaken with blood from the general and from the portal circulation have been negative. Some observers claim to have obtained evidence of improvement in sugar utilization, but their claims have not been confirmed.

The recent work of Verzar and of Murlin and Kramer firmly establish that pancreatic extracts are no more effective. The conditions in the parabiosis experiments of Sauerbruch and of Forschbach are too complicated to permit of undisputed deductions. By uniting the circulations of a normal and a diabetic dog the authors observed a decrease of glycosuria in the diabetic animal, although the normal animal became glycosuric. Hedon made the interesting observation that when the pancreas

of a normal dog with its vascular attachment preserved is transplanted between the carotid artery and jugular vein of a diabetic dog the glycosuria remains uninfluenced. However, when the anastomosis is made with the splenic artery and vein, the glycosuria is greatly decreased, to return with the former severity when the animals are separated. Hedon then found that though blood from the pancreatic vein of a normal animal injected into the general circulation of a diabetic animal did not appreciably influence the glycosuria, when injected into a mesenteric vein the glycosuria was markedly decreased. The technical difficulties of such experiments are so great and the conditions surrounding them so complex that inferences must be drawn with great care. The implications of Hedon's experiments are obvious, but so far as I know the observations have not been confirmed.

It is generally conceded that the source of the pancreatic influence over sugar metabolism resides in the islands of Langerhans. Schaefer suggests this view in 1895, and it was elaborated by Opie. However, there is by no means accord upon this point among pathologic anatomists. Hansemann still champions the acinous theory, although he stands alone, while those authors with widest experience—Opie, Weichelsbaum, Sauerbruch, MacCallum, and many others—adhere to the insular theory. In recent years prominent pathologists, among them Reitmann, Herxheimer, Fahr, have accepted the view that the islands of Langerhans do not represent independent structures. They find so many transition forms between acini and islands that they believe one may under certain conditions be transformed into the other. Perhaps the strongest support of the island theory was the observation that tying the pancreatic duct which does not produce glycosuria leads to atrophy of the acini, but leaves the islands intact. However, Pratt finds the islands degenerate as well as the acini, and though glycosuria does not develop, sugar tolerance is reduced. Homans has recently added valuable evidence to the island theory by studying the islands in the piece of gland left after partial removal of the pancreas in cats. In those animals which fail to develop

diabetes the disappearance of secretory granules in the islands suggests overactivity; in those developing diabetes he finds degeneration of the islands without disturbance of the remaining acinous tissue. Embroyologic and histologic studies indicate the structural independence of islands and acini.

In pancreatic diabetes there is both an increased production of sugar and a loss of the tissue power to utilize sugar, but which of the two is the primary and essential factor has long been controverted. That sugar introduced subcutaneously is quantitatively excreted and the constant dextrose-nitrogen ratio point against any utilization of sugar. However, certain arguments have been advanced in favor of a partial combustion in pancreatic diabetes. First, sugar given by the mouth is not always quantitatively excreted. It is possible that some sugar is lost by decomposition or remains temporarily stored in the body. At any rate, the force of this argument is lost, since calorimetric experiments fail to indicate any rise in the respiratory quotient. Second, phloridzin and adrenalin increase the glycosuria. This argument is hardly of importance, since the mechanism of phloridzin and adrenalin diabetes is not fully understood. It is quite probable that their point of attack is different from that of the pancreas. Third, the failure of acidosis in depancreatized dogs. Brugsch particularly has pointed to this as the chief distinguishing feature between human and experimental diabetes. In this statement the different dietary habits of man and dog are not sufficiently weighed, and later experiments have shown that acidosis is by no means rare in dogs. Fourth, muscular exercise decreases the glycosuria and raises the respiratory quotient. Seo has shown that this occurs only when the pancreas has not been totally removed. Fifth, cold increases the glycosuria. Allard fails to confirm this observation, and Luthje explains it by assuming an increased production of sugar from protein which is then excreted instead of being burned.

All of the evidence then points against any sugar utilization in the tissues of animals with pancreatic diabetes, and these results have been established likewise for severe diabetes in man. Whether this inability to utilize sugar resides in the tis-

sues themselves or in some alteration in the sugar that is presented to them remains undetermined. Porges and Solomon found that after cutting off the circulation below the diaphragm of pancreëctomized dogs, the respiratory quotient rose to one—indicating that sugar was then being burned in the muscles. They explain the constantly low respiratory quotient in diabetes by assuming that during the transformation of protein and fat into sugar, bodies with a very low respiratory quotient are formed, and though sugar is burned in the tissues, still these bodies hold the quotient down. Since the liver is the organ where protein and fat conversion into sugar occurs, eliminating the liver immediately raises the quotient to the sugar level. The main importance of this experiment is that von Noorden gives it prominence in his latest theory of diabetes. However, the results of Porges and Solomon lose all value before the withering criticism of Rolly and David.

Pancreatic diabetes is the only experimental form of glycosuria that bears any similarity to the disease diabetes mellitus. However, a consideration of pancreatic influence by no means exhausts the possibilities of carbohydrate metabolism, for although the pancreas is the dominant regulator, other glands play a not insignificant rôle.

Blum in 1901 noted glycosuria after the subcutaneous and intravenous injection of epinephrin. Subsequent observations have shown that the glycosuria lasts as long as epinephrin is present in the blood, and that the degree of glycosuria is roughly parallel with the epinephrin concentration. Subcutaneous and intraperitoneal injections cause a more marked glycosuria than intravenous injections, but a continuous inflow of very dilute epinephrin will establish and maintain glycosuria. After continuous or repeated injections glycosuria fails to occur, although hyperglycemia persists. Pollock ascribes this to changes in renal function. Epinephrin produces its most marked effect when a glycogen reserve is present, but it causes glycosuria in starving animals and increases the glycosuria at the height of pancreatic diabetes and in human diabetes. However, if the pancreas and adrenals are removed in dogs, glycosuria does not

occur. It is said that under the influence of epinephrin the muscle glycogen disappears before the liver glycogen, which is the reverse of all other forms of glycosuria. Epinephrin causes glycosuria in fasting dogs. This sugar is formed from protein, and Eppinger, Falta, and Rudinger have demonstrated an increased protein katabolism. However, Ringer and Lusk have been unable to confirm this observation. In contradistinction to pancreatic diabetes, the hyperglycemia caused by epinephrin is associated with an increased combustion of sugar. Paton states that while glucose facilitates the action of epinephrin, levulose has not the same effect. In dogs with the adrenals removed and in Addison's disease there is a low blood-sugar, increased tolerance for glucose, and an absence of glycosuria after epinephrin.

The point of action of epinephrin is certainly upon the terminals of the sympathetics in the liver. This is in accord with the general law of its action. It is further supported by the observation of Loewis, that chrysotoxin which inhibits the sympathetic control likewise inhibits the action of epinephrin and that ergotoxin also diminishes its action. MacLeod and Pearce have shown that a stimulation of the splanchnics causes hyperglycemia; if the adrenals are removed or the liver completely denervated, hyperglycemia does not follow such stimulation. Therefore, they conclude that while epinephrin is absolutely necessary for stimulation of the splanchnics to be effective, still the effects of stimulation depend upon something more than an increased discharge of epinephrin.

Similar to the effect of the adrenals upon carbohydrate metabolism is the action of the hypophysis. Injections of the extract cause glycosuria, increased protein katabolism, and a rise in the respiratory quotient indicating sugar consumption. Cushing and his co-workers have shown that electric or mechanical stimulation of the hypophysis causes glycosuria, followed by a period of decreased carbohydrate tolerance, and that removal of the gland is followed by increased sugar tolerance and a tendency to put on fat.

Eppinger, Falta, and Rudinger have given a prominent place

to the thyroid and parathyroid glands in carbohydrate metabolism. In thyroidectomized dogs they find the protein metabolism reduced and the protein-saving qualities of sugar and fat diminished; feeding thyroid again increases the protein metabolism and restores the normal protein-sparing property of sugar and fat. The glycosuric action of epinephrin is lost, but is again restored by prolonged thyroid feeding. Phloridzin acts quantitatively and qualitatively as in normal dogs. In contradistinction to the effects of removal of the pancreas alone, removal of the thyroid and pancreas leads to no increase of protein metabolism; the dextrose nitrogen ratio equals 3.5; and the loss of weight of hungering animals is less rapid. In thyroidectomized dogs, piqure fails to produce glycosuria. The parathyroids, according to these authors, have an action opposed to thyroid. If parathyroids and thyroid are removed, epinephrin produces glycosuria as normally and the assimilation limit for sugar is greatly decreased. If the parathyroids alone are removed, there is a great reduction in sugar tolerance and the protein metabolism remains unaffected. When the pancreas and several parathyroids are removed, the dextrose-nitrogen ratio rises to 3.5—but in contradistinction to the conditions following pancreas and thyroid removal, the protein metabolism is increased as it is when the pancreas alone is removed. In the pancreas-thyroid experiments the amount of sugar excreted was the same as when the pancreas alone was removed, and Eppinger, Falta, and Rudinger explain the high dextrose nitrogen ratio by the lowered protein metabolism due to the removal of the thyroid. These results upon the influence of the thyroid and parathyroid upon carbohydrate metabolism have been severely critized. Underhill and Saiki found that dogs with the thyroid removed tolerated little sugar subcutaneously, results which Eppinger, Falta, and Rudinger insist are due to removal of the parathyroids with the thyroid. Underhill has produced epinephrin glycosuria in thyroidectomized dogs with two parathyroids remaining. Ritzmann claims that the loss of epinephrin glycosuria is only one of the many immediate effects of thyroidectomy, and that after a few days the glycosuric property

of epinephrin is restored. On the other hand, McCurdy finds that if the thyroid be removed and the parathyroids remain there is a permanently increased tolerance for sugar, and MacCallum's experiments indicate a reduction in the glycosuria of pancreëctomized dogs when the thyroid is subsequently removed.

In all experimental work in diabetes and perhaps still more strikingly in clinical observations the importance of a nervous element in glycosuria has been recognized. Claude Bernard showed that a stab into the floor of the fourth ventricle at the apex of the calamus scriptorium caused transient glycosuria. The results of the piqûre depend upon the glycogen reserve in the liver, for if the liver be rendered glycogen-free, glycosuria fails to appear. The impulse from the brain to the liver is conducted through the sympathetic, for section of the sympathetic cord prevents glycosuria after piqûre. Further, it has been found that section of the left splanchnic prevents glycosuria just as section of the sympathetic cord does. The left splanchnic supplies both adrenals. When the adrenals are removed, piqûre is without effect. This evidence implicating the adrenals as an essential link in the mechanism of piqûre glycosuria is further supported by the observations of Stewart, who finds an increased outflow of epinephrin from the gland after splanchnic stimulation, and the histologic studies of Kohn, which point to increased activity of the chromaffin cells after splanchnic stimulation. Evidence from older experiments indicates that piqûre is effective when all the nerves to the liver are cut, but MacLeod and Pearce have shown that when the denervation is complete splanchnic stimulation only occasionally leads to hyperglycemia. Therefore, while epinephrin is apparently essential for sugar mobilization, still these authors think splanchnic stimulation exercises a direct influence upon the liver. Of the greatest importance are the studies of Cannon and his co-workers, who find emotional states such as fright are accompanied by an increased secretion of epinephrin, and not infrequently with glycosuria.

The whole question of nervous glycosuria and particularly of the glycosuria associated with cerebral injury and disease needs

revision in the light of Cushing's experiments upon the hypophysis. As he has pointed out, the Claude Bernard piqûre is very close to the hypophysis, and puncture of the hypophysis has the same effect as the classical piqûre. Stimulation of the superior cervical sympathetic ganglion causes glycosuria even if all possible paths of downward conduction are cut, and even after connection with the central nervous system is destroyed by nicotin. When the hypophysis is removed, stimulation of the superior cervical sympathic ganglion fails to give glycosuria. A Bernard piqûre will cause glycosuria even after transection of the cord above the emergence of the splanchnics. The general experimental evidence would indicate that under nerve stimulation the adrenals react more promptly than the hypophysis in producing glycosuria, but that the latter gland may function in the same way as the chromaffin tissue does. What interrelation there may be in their function remains unexplained.

On the basis of the interaction of the ductless glands in regulating carbohydrate metabolism an elaborate theory of diabetes has been erected. Much of this work has been done by von Noorden's pupils and it has received the stamp of his approval. The theory is applied in detail in the last edition of his book on diabetes. A fundamental basis of the conception rests upon the experiments of Porges and Solomon which have been recorded. The deduction from the experiments is that the diabetic organism is able to burn sugar just as the normal organism does, and that experimental pancreatic diabetes, as well as the disease in man, is primarily an overproduction of sugar and not an inability to utilize it.

Normally, the glycogen reserve of the liver is consumed in response to the needs of the body, and as the glycogen is used up, a fresh supply is manufactured from the food. The pancreas is the great controller of this process, the damper that holds it within appropriate bounds. When its regulating influence is removed, sugar production goes on in an unrestrained and inordinate way, the blood is flooded with glucose, and sugar flows off in the urine. The chromaffin system is the important sugar

mobilizer. Its action is opposed to that of the pancreas. Normal carbohydrate metabolism is the result of a balance between these two forces. Nervous influences play an important part by stimulating the adrenals and other endocrine glands play their part by either exciting or depressing the function of the pancreas or adrenals. Thus, the thyroid augments the adrenals, while it inhibits the pancreatic function. Therefore, when the thyroids are removed, pancreatic glycosuria is diminished; when the gland is hyperactive, glycosuria readily occurs. Reversely, if the pancreas be removed its depressing action upon the thyroid is released, the thyroid then forcing up the general metabolism and thus producing the increased protein metabolism characteristic of pancreatic diabetes. In like manner the relation of the parathyroids and of the hypophysis in this schema may be easily deduced. In a broad way the pancreas and parathyroids presumably depress carbohydrate metabolism, while the chromaffin tissue, thyroid, and hypophysis facilitate mobilization. Diabetes, therefore, is no single entity, for if any chain in this complex system of regulation be impaired, the co-ordination of activity of all the endocrine glands is deranged.

There is no evading the fascination of this hypothesis, and though persuaded of the inaccuracy of much of its foundation, still it is difficult to disregard its charm. It lends itself admirably to diagrammatic representation, it allows of complex and yet clear explanation of many of the otherwise unexplained facts of carbohydrate metabolism, and it encourages endless even though vague and fanciful speculation. It is well to insist, as has been already pointed out, upon the firmly established fact that the primary and essential feature of diabetes is an inability to utilize sugar. All else is secondary to this deficiency. The hyperglycemia, the glycosuria, the glycogen depletion, and increased glyconeogenesis are in response to a constant demand of the tissues for more sugar which they cannot use. What part the endocrine glands other than the pancreas may play in this fruitless and distorted mobilization is still undetermined.

Although the explanation of the nature of diabetes upon the basis of interaction of the endocrine glands is quite inadequate

to meet the facts, still the observations that have been made upon their influence upon metabolism have shed considerable light upon their function and have given valuable points to the clinical interpretation of their derangements. Individuals normally vary in their response to alimentary tests of sugar tolerance, but the range of variation is relatively small, and any gross departure from the usual limits has an important clinical significance. A tolerance reduced so low that sugar occasionally appears in the urine upon an ordinary diet does not always mean diabetes. It is true that the distinction here requires the most refined clinical interpretation, for diabetes no doubt often begins as an alimentary glycosuria, and passes gradually through the stage of glycosuria following starch ingestion, and finally to glycosuria upon a purely protein diet. The importance of early diagnosis in diabetes I have sufficiently emphasized, but the stress will bear repetition, since there is every reason to believe that judicious dietary management will postpone and in some instances possibly avert the later and serious stages of the disease. But occasional glycosuria should prompt us to review carefully all possible sources of carbohydrate metabolism derangement, and a suspicion of disease of some of the endocrine glands may find considerable support from an estimation of the glucose tolerance. As a rule, decrease of carbohydrate tolerance is accompanied by loss of weight, and an increase by an excessive decomposition of fat.

Of all the endocrine glands other than the pancreas, the thyroid exercises the most significant control over metabolism. Hyperthyroidism is nearly always associated with an increased metabolism, emaciation, and a lowered carbohydrate tolerance. Occasionally sugar appears in the urine on a mixed diet, and epinephrin glycosuria is easily induced. The combination of Graves' disease and diabetes has been occasionally described, but in this association the diabetes runs its course independently of variations in the thyroid symptoms. Feeding thyroid to normal individuals or animals reduces sugar tolerance and occasionally leads to spontaneous glycosuria.

In myxedema, the carbohydrate metabolism factors are the

reverse of those in Graves' disease. The basal metabolism is reduced, sugar tolerance is increased, and an accumulation of fat is strikingly characteristic. The tendency to epinephrin glycosuria is markedly reduced.

It must not be inferred that all instances of derangement of thyroid function fall regularly as regards sugar tolerance into one of these two groups. Such an inference would be opposed to all our clinical experience with disease of the thyroid gland. It is well known how irregularly the symptoms of abnormal thyroid function are grouped. Sometimes autonomic symptoms predominate, sometimes sympathicotonic, sometimes the two vary in different domains; hyperthyroidism may be followed by hypothyroidism or the reverse; and not infrequently symptoms of hyper- and hypothyroidism are conjoined. This variation explains why sometimes a clinical picture of predominating hyperthyroidism is associated with increased sugar tolerance, why an increased tolerance may be replaced by decreased tolerance, or vice versa, and how in rare instances diabetes is associated with outspoken symptoms of myxedema. Falta, who, as I have previously stated, regards the action of the thyroid as opposed to the pancreas function, believes that much of the irregularity that exists depends upon the functional range of the pancreas. If the range be wide, the thyroid will influence carbohydrate tolerance but little, whereas, if it be small, the thyroid influence will easily be asserted.

The experimental work of Cushing has shown the intimate relation between hypophysis function and glycosuria and obesity. As is well known, the pituitary body consists of two separate glands which are distinct embryologically, histologically, and physiologically. The anterior portion or pituitary gland is developed from the epithelium of the buccal cavity; the posterior portion or hypophysis from cells of the central nervous system. The pituitary exercises a marked influence upon growth and development, but apparently only the hypophysis is concerned in carbohydrate metabolism. However, it has long been known that overfunction of the pituitary is frequently associated with overfunction of the hypophysis, and the association of acro-

megaly and diabetes was commented upon by Marie. Borchardt collected 176 cases of acromegaly from the literature, and found diabetes to be present in 63, and in 8 more alimentary glycosuria had been noted. Sometimes the diabetes is of a severe type and leads to death, but more often it is of a mild form, and there may be lack of correspondence between carbohydrate ingestion and sugar excretion.

The relation of sugar tolerance to disease of the hypophysis shows great variation, just as it does in relation to disease of the thyroid. As a rule, when other distinct symptoms of hyperpituitarism are present, the tolerance is low; when other symptoms point definitely to hypopituitarism, it is high. But as symptoms of acromegaly frequently culminate in a clinical picture of hypopituitarism, so glycosuria may be replaced ultimately by a high sugar tolerance, and during the transition stages the carbohydrate relation may vary from time to time. The absence of a constant relation between carbohydrate metabolism and hypophyseal disease, for instance, a high sugar tolerance associated with acromegalic features, has proved an unsolvable puzzle to many clinicians. Indeed, Allen, largely upon this basis, denies the hypophysis any specific control over carbohydrate metabolism. However, that such apparent contradictions should exist must appear quite reasonable.

The only clinical complex associated with deficiency of the adrenals is Addison's disease. In this condition the blood-sugar is usually low, epinephrin glycosuria is absent, and sugar tolerance is high. Emaciation is the rule, but this is probably the result of the digestive disturbances rather than of deranged metabolism. The interpretation of the clinical symptoms of Addison's disease is complicated by the complex structure of the adrenal glands. The cortex is interrenal tissue derived from the mesothelial cells of the genital ridge; the medulla is chromaffin tissue derived from the nervous system. While there is reason to believe that the chromaffin tissue furnishes the secretion that influences the carbohydrate metabolism, it is probable that the cortex is responsible for some of the symptoms of Addison's disease.

Conditions of hyperfunction of the chromaffin tissue have no sound clinical foundation. The attempt to associate the hypertension of nephritis with hyperepinephrinemia have not been successful. Instances of true adrenal diabetes are unknown.

From what has been said thus far you must see that glycosuria is not peculiar to diabetes, that it is not fair to conclude that every patient with sugar in the urine has diabetes. Sugar in small amounts may be found in the urine in a variety of conditions, and it often requires very careful investigation before one can make a definite decision. Since reduction tests are almost exclusively used to detect sugar in the urine, we must first of all be sure when only slight reduction occurs that the reaction is due to sugar and not to some other substance. We must further determine that the glycosuria is associated with hyperglycemia and is not due to abnormal renal permeability. Finally, if indeed the condition be a genuine hyperglycemic glycosuria, we must by careful clinical study decide whether the condition be due to mild diabetes or to disturbed function of one or more of the ductless glands, for instance, to thyroid or hypophyseal disease. I hesitate to comment upon so trite a matter as the proper directions to give patients when asking for specimens of urine, and I should not do so were I not convinced by experience of the tremendous importance of this apparently trivial matter. If you ask patients for a specimen of urine, almost invariably will they bring a portion of the urine passed upon arising. From the standpoint of detecting a small amount of sugar this is the least desirable specimen of the twenty-four hours. In the early stages of diabetes and in mild forms of the disease glycosuria occurs only transiently after meals. The best specimen to examine is the urine passed from two to four hours after the largest meal of the day. It is important, therefore, as a routine, to instruct all patients to send two specimens of urine, one from the night voiding passed a few hours after dinner, the other from the early morning voiding. I have known of mild cases of diabetes overlooked in spite of repeated urine examinations because the specimen examined was always from the morning voiding, and each year I detect 5 or 6 mild cases of diabetes with sugar

in the evening specimen and none in the morning. Besides the question of discovering glycosuria, the routine practice of examining morning and evening specimens has other advantages. The evening specimen often contains a little albumin and a few casts when the morning specimen contains neither, and in cases of nephritis the two specimens frequently show such a wide difference of specific gravity that an important estimate of renal function is at once obtained.

For the practising physician the readiest and most satisfactory test to confirm the presence of sugar when there is slight reduction is the fermentation test, and this additional evidence should never be neglected. If the reduction be due to sugar, we must proceed further and determine the relation of the blood-sugar to the glycosuria. We have proposed a relatively simple test to determine this that gives a quicker and more satisfactory insight into the carbohydrate metabolism of a patient than any other method with which I am familiar. The test consists in studying the fasting blood-sugar and the blood-sugar and urine one-half hour, one hour, and two hours after administering 100 grams of glucose. I cannot go into details of the test; briefly, in normal persons the blood-sugar mounts only a little, and soon returns to the fasting level, whereas, in diabetics the blood-sugar goes much higher and the rise is longer sustained. In normal persons sugar appears in the urine if the blood-sugar reaches 0.18 per cent. Mild forms of renal diabetes are frequently disclosed by this method, and it is important to distinguish these from mild forms of diabetes.

In the few remaining minutes I must compress my remarks upon one of the most important aspects of carbohydrate metabolism, one well deserving a much more extended consideration. I have already emphasized the fact that although fat is built up largely from sugar, this process is apparently not reversible, since evidence points distinctly against fat being a source of sugar. Glycerin is certainly converted into sugar, but the fatty acids are not. All fatty acids found in the human body have an even number of carbon atoms, and since the splitting of fat occurs always at the next to the last carbon atom, when the

splitting has proceeded far enough, a molecule of β-oxybutyric acid is formed. I have already pointed out that those amino-acids which are not converted into sugar are easily converted into β-oxybutyric acid. This acid body, therefore, comes both from protein and from fat, but by far the larger amount comes from fat. The tremendous disturbance of fat metabolism in severe diabetes is often indicated by the large amount of fat in the blood. It would appear that the need for carbohydrate is so great that the transportation of fat from the subcutaneous depots is stimulated far beyond the capacity of the organ or organs concerned in its burning. It must not be thought that protein and fat metabolism follow abnormal channels in diabetes; all the evidence is against this view. However, in some curious and unknown way the satisfactory burning of β-oxybutyric acid requires the concomitant burning of sugar. In starvation, aceto-acetic acid and acetone rapidly appear in the urine, to disappear promptly upon the administration of carbohydrate. In diabetes, these acid bodies, instead of being burned, frequently accumulate in the body, upset the acid-base equilibrium, and cause the serious and dangerous group of symptoms known as acidosis.

A fundamental requisite for the proper transaction of metabolic affairs is a fine adjustment of the reaction of the body juices. The reaction may vary only within a small margin, and since acids are taken into the body in great excess of bases, the body must possess an efficient machinery to maintain a constant reaction. Bases must be present to neutralize acids as rapidly as they are formed, and there must be a way of eliminating acids while bases are retained, or the supply of base would soon be exhausted. When the supply of base is exhausted a fatal intoxication occurs.

The body possesses an admirable machinery to meet these demands. There are three ways in which it protects itself against an overwhelming accumulation of acid:

1. The blood is so constituted that a large amount of acid or alkali may be added to it without changing the reaction.

2. A large amount of acid is eliminated through the lungs and kidneys.

3. A large amount of the ammonia formed in the body may be used to neutralize acid.

As Henderson and Palmer have pointed out, the blood represents a remarkably suitable mixture to maintain a constant reaction. Owing to the ready adjustment between the proportion of carbonates and bicarbonates and between the proportion of mono- and dibasic phosphates, large amounts of acid or alkali may be absorbed without altering the reaction. The proteins also may absorb a considerable amount of acid without changing reaction.

The lungs excrete large amounts of carbon dioxid. In the lung, carbon dioxid is given off from the carbonates which are returned to the tissues as bicarbonates, which there absorb carbon dioxid and return again to the lungs as carbonate. If the amount of acid in the blood rises, this free play between carbonate and bicarbonate is interfered with. Much of the bicarbonate is removed to hold the acid, so that carbon dioxid accumulates in the tissues and in the blood; the carbon dioxid tension in the lungs falls; and the stimulation of the respiratory center by the retained carbon dioxid produces increased ventilation of the lungs in an effort to restore the balance.

The kidneys have the very remarkable power to separate an acid secretion from a faintly alkaline mixture, and in this way a large amount of acid is excreted from the body while valuable alkali is retained.

Finally, a large amount of ammonia is formed in the body from the decomposition of protein. Normally, most of this ammonia combines with carbon dioxid to form urea, but in the presence of an excess of acid much of it may be diverted to neutralize this acid, which is then excreted by the kidney as an ammonium salt.

We now possess numerous clinical methods to detect when the acid equilibrium mechanism of the body is disturbed, when it is being taxed, and when it is approaching exhaustion. The stage of exhaustion is readily appreciated by the profound alteration

in the character of the respiration known as air hunger, and serious manifestations of intoxication by the nervous system, chiefly coma. But long before these dangerous symptoms arise, relatively innocent changes point to a warning. In diabetes, abnormal acid bodies may be present in the urine as the earliest indication of an excessive acid accumulation, and an important object in treatment is to control metabolism so that these bodies are permanently absent from the urine. A decrease of bicarbonate in the blood may be measured either directly or in terms of the carbon dioxid tension in the alveolar air. The total alkali reserve of the body may be approximated by measuring the bicarbonate tolerance. The ammonia diversion may be measured by estimating the ammonia nitrogen in the urine. Finally, the reaction of the blood may be discovered by determining the hydrogen-ion concentration of the dialysate and its so-called buffer value.

For practical purposes the two methods usually employed are to examine the urine for aceto-acetic acid and acetone and to follow the carbon dioxid tension in the alveolar air. These two methods yield the greatest amount of information for the least outlay of time and skill. If a third is to be added, the estimation of the ammonia nitrogen in the urine is to be recommended.

SEROUS MEMBRANE TUBERCULOSIS

L. G., age fourteen; male; black; single.

The patient entered the hospital on December 13, 1918, complaining of swelling of the stomach.

Family History.—Unimportant.

Past History.—The boy's general health has been good, though he has never been robust. Whooping-cough at five years and measles at seven years the only infections. No history of cough. Appetite and digestion good.

Present Illness.—About December 1st the patient began to feel drowsy and tired, and to sit in the house instead of running out and playing with the other boys. He became steadily worse, and a few days later his mother noticed that his abdomen was swelling. Since then his condition has grown progressively worse. He feels chilly in the evening and has fever, and the abdomen has steadily increased in size.

Physical Examination.—Temperature 101° F. Pulse 136. Respirations 44. Blood-pressure 110/80. The patient is markedly underdeveloped and undernourished. Respirations are rapid. Slight unproductive cough. Mentally dull. Examination of the head showed no noteworthy abnormality. No glandular enlargement. *Lungs:* The lower borders have a high position and in the left axilla a friction-rub is heard. The *heart* shows no abnormality. *Abdomen:* Greatly distended. Skin is shiny and tense. Small umbilical hernia. Marked fluid wave and shifting dulness. General tenderness.

Laboratory Findings.—Blood: Hb. 70 per cent. R. B. C. 5,664,000. W. B. C. 7400. Differential count essentially normal. *Urine:* Essentially normal. *Stools:* Show no abnormality. Wassermann negative.

On December 14, 1918, 4 liters of clear, serous fluid were removed from the abdomen. After tapping the spleen was palpable, the abdominal wall was still held tensely, and there

was resistance in the right lower quadrant, but no mass could be made out. The *x*-ray report December 17th, 1918, shows pleural thickening at left base, with high position of the diaphragm on both sides.

Course in Hospital.—After admission to the hospital the patient continued to run a high, irregular fever. The leukocytes have remained in the neighborhood of 8000. The abdominal swelling has decreased somewhat. The patient has lost weight and has become very emaciated. On January 8, 1919, a friction-rub was noted in the lower right axilla. On March 12th a large pleural effusion was discovered on the right side. The von Pirquet tuberculin test is positive.

Mr. ——— has given the history of this patient, and the situation presents no diagnostic difficulty. The colored boy has been in the hospital about two months, and during his residence here has shown this irregular fever, with rapid pulse. The abdomen now is not very prominent; it is a little tender and quite tense, but there is no muscle spasm. There is a small amount of free fluid. Here between the costal margin and the umbilicus is an indefinite transverse mass. These abdominal symptoms were present on admission, although they have changed somewhat; that is, the amount of fluid has lessened and the resistance in the epigastrium has gradually developed. During his stay in the hospital a pleural friction-rub was observed on the left side, and later on the right side. The boy now has a marked pleural effusion on the left side, as is well shown in these *x*-ray plates.

The diagnosis of tuberculous peritonitis is not always as easy as it is in this case, although the diagnosis is usually not so difficult in children as in adults. For practical purposes it is convenient to divide tuberculous peritonitis into the ascitic and the dry forms. In children the ascitic form, when accompanied by fever, offers no obstacles to diagnosis. The only conditions with which it might be confused are—

1. Certain unusual instances in emaciated infants when fluid in the intestines is mistaken for fluid in the peritoneal cavity.

2. Thrombosis of portal vein. The condition is not common and the history usually distinguishes it.

3. In the older literature much is written about an idiopathic form of peritonitis that comes on insidiously in adolescence, particularly in girls. With slight or no constitutional symptoms a peritoneal effusion gradually develops which lasts a short time and then slowly disappears. All such cases that have been operated upon were shown to be tuberculous, and it is only reasonable to assume that they are tuberculous.

In adults the diagnosis of the ascitic form is further complicated by its resemblance to cirrhosis of the liver and carcinomatosis of the peritoneum. Even at operation the differentiation between carcinoma and tuberculosis of the peritoneum may remain in doubt until microscopic examination of sections of an excised nodule decides the difficulty. During the past winter you have seen cases in the wards where it was impossible to decide definitely between the three conditions. Where there are in addition to ascites marked constitutional symptoms, and abdominal tenderness and pain, the diagnosis is usually clear. If, in addition to the peritoneal manifestations, there are also signs of pleural or pericardial involvement, the diagnosis is certain. In doubtful cases, the presence of a definite tuberculous focus elsewhere, for instance, in the lungs or testicles, may establish the diagnosis. The differentiation of tuberculous peritonitis from cirrhosis of the liver is especially difficult because the two conditions are so frequently associated. In the terminal stages of cirrhosis, tuberculous peritonitis is often added.

In the dry form of tuberculous peritonitis the diagnosis is beset with greater difficulties. When the symptoms come on acutely they may be mistaken for appendicitis or cholecystitis. The hospital records of the surgical side show many instances operated upon under such mistaken impressions. Four or five patients have been operated upon for intestinal obstruction, and tuberculous peritonitis quite unexpectedly discovered at operation. In still another group operated upon for hernia the peritoneum was found studded with tubercles, sometimes the hernial sac alone being involved.

Of special interest are the curious abdominal tumors that are often found and which not infrequently mislead. These tumors are formed—

1. By the rolled-up omentum.
2. By encapsulated fluid.
3. By matted intestines.
4. By enlarged glands.
5. By pelvic masses.

The commonest abdominal tumor is the rolled-up omentum. It forms a characteristic boggy, ill-defined mass stretching transversely across the abdomen a little above the umbilicus. Encapsulated fluid may simulate a cyst, and this error in diagnosis has frequently been made. Spencer Wells operated upon a patient for ovarian cyst. The condition was found to be an encapsulated tuberculous exudate, and the patient recovered so satisfactorily and unexpectedly that operation was advised for tuberculous peritonitis, and this method of treatment has remained popular to this day. Coiled intestines form indefinite boggy masses that are quite characteristic. They are often multiple. Sometimes the whole small intestine is coiled up as an adherent mass in the region of the umbilicus. Tumors formed of enlarged retroperitoneal and mesenteric glands are rarely encountered in adults. Even in children they are uncommon. Pelvic masses, strictly speaking, should not be included in peritoneal tumors. However, I do include them on account of their frequent occurrence and their importance. The usual sequence of events is that a diagnosis of pelvic inflammatory disease is made; the patient is operated upon, and unexpectedly the peritoneum is found studded with tubercles; the pelvic mass is found also to be tuberculous and is removed; the patient makes a satisfactory and a complete recovery. It is just these cases that have given such great prestige to the operative treatment of tuberculous peritonitis.

In considering tuberculous peritonitis I wish to view the condition from three different angles:

1. As a local tuberculous disease, just as one speaks of pulmonary tuberculosis as a local tuberculous disease.

2. As one manifestation of the whole course of tuberculous infection.

3. As a part of a disease affecting the large serous cavities.

Of tuberculous peritonitis as a local disease I may say that it is a very serious and grave tuberculous manifestation. In this respect it contrasts markedly with tuberculous pleurisy, which is one of the mildest tuberculous manifestations. It occurs more commonly in children than in adults, but the difference in this respect is not extreme. I have already spoken of the general clinical features and the diagnosis of the condition. The prognosis is always grave, although many cases and even some very severe and complicated cases recover. Some years ago I investigated the subsequent history of all the patients with tuberculous peritonitis who had been in the hospital. The immediate results are as follows:

Discharged from the hospital as well.....16 cases.
Discharged improved.....71 "
Discharged unimproved.....15 "
Died.....48 "

This gives an immediate mortality of 32 per cent. in all cases. The gynecologists had by far the best record—only 5 deaths in 48 cases, or 10 per cent.

An effort was made to discover the subsequent results in the patients leaving the hospital. All were written to, and those living in the city were personally hunted up and visited. From Dr. Bloodgood I obtained the after-results in a number of the surgical cases. In all, 43 cases were heard from. Of these,

14 were reported dead.....33 per cent.
7 were reported living, but not well.....16 " "
22 were reported living and quite well.....51 " "

Of the 14 cases reported dead,

3 died within three months.
1 died within one year.
3 died within two years.
1 died after one year from acute intestinal obstruction.
1 died after three years from carcinoma.
1 died after two years from an operation said to have been for gall-stones.

Of the 7 living, but not well,

1 was living after ten years. Feels strong and well, but sinus persists.
1 was living after six years, but has tuberculous glands in the neck.
1 was living after six years; has attacks of abdominal pain, but is otherwise well.
1 was living after six years; writes that she is thin and weak.
1 was living after four years with a persisting sinus.
1 was living after two years with a persisting sinus.
1 was living after one year, but with a swollen abdomen and enlarged liver.

Of the 22 living and well,

2 cases	living	and	well	after	ten	years.
1 case	"	"	"	"	eight	"
2 cases	"	"	"	"	seven	"
1 case	"	"	"	"	six	"
1 case	"	"	"	"	five	"
2 cases	"	"	"	"	four	"
6 cases	"	"	"	"	three	"
4 cases	"	"	"	"	two	"
3 cases	"	"	"	"	one year.	

Tuberculous peritonitis is then a very fatal disease; and even when there is improvement, the after-results are not very brilliant. Still, one can never say what the outcome will be in a given case, and some of the least promising turn out the best. One of the cases that recovered had, besides the peritonitis, pleurisy with effusion, pneumothorax, and tubercle bacilli in the sputum.

The only point in the treatment of tuberculous peritonitis that deserves special consideration is the question of operation. You will find if you investigate the matter that opinion is divided. And, indeed, it has always appeared to me that the question of the value of operation cannot possibly be settled on the basis of the data at present available. The statistics that have been published are very unsatisfactory. Those who advocate operation admit that only selected cases are suitable for operation, and the cases they select happen to be the very cases that

do best under medical treatment. How unreasonable to compare results obtained on selected cases with results obtained on all cases. Cases of tuberculous peritonitis accidentally discovered at operation are nearly always very mild cases, indeed, many of them never give symptoms. These two are included among surgical cases. I must say that I am not enthusiastic about operation, for I feel that no satisfactory proof of the value of operation has been offered. The only group of physicians who get good results in the treatment of tuberculous peritonitis are the gynecologists. In their cases the tuberculous pelvic disease is the important thing; the tuberculous peritonitis, which is often local, is incidental. When the large pelvic tuberculous masses are removed the tuberculous peritonitis heals readily.

Before speaking of tuberculous peritonitis as a manifestation of tuberculous infection in the individual and of tuberculous peritonitis as a part of a general serous membrane disease, I wish to show the second patient:

R. G.; age fourteen; male; black; single.

The patient entered the Johns Hopkins Hospital on February 17th, complaining of pain around the heart.

Family History.—Gives no details of interest.

Past History.—The patient has always been healthy up to onset of present illness. He has suffered from many attacks of sore throat. As a child he had pneumonia. He thinks he has lost some weight.

Present Illness.—One month before admission to the hospital the patient noticed pain over the heart and shortness of breath. The pain became worse, but the shortness of breath did not increase. There was loss of appetite, some nausea, and on one occasion vomiting. The pain gradually became so bad that one week ago the patient was obliged to leave school and go to bed. For the past week he has had a sweat each night. He has noticed no particular loss of strength.

Physical Examination.—Temperature 100.4° F. Pulse 94. Respirations 22. Blood-pressure 114/70. Fairly well-nourished colored boy, a little apathetic. Mucous membranes pale.

Large, scarred tonsils, with large glands at angle of jaw. Fairly marked general glandular enlargement, including epitrochlears. *Heart:* Slight wavy precordial impulse. The area of cardiac dulness is increased; it extends 4 cm. to the right and 16 cm. to the left of the median line. The area of dulness extends upward in a triangular shape. The heart sounds are clear, but distant. Loud to-and-fro friction to the left of the sternum. *Lungs:* At the left base there is a little impairment and distant breath sounds due to pulmonary compression. *Abdomen:* Shows no noteworthy abnormality.

Laboratory Findings.—Blood: Hb. 60 per cent. R. B. C. 4,420,000. W. B. C. 9400. The differential count is essentially normal. Wassermann reaction negative. *Stool* negative.

Course in Hospital.—During the patient's stay in the hospital he has run an irregular fever and a rapid pulse. The temperature has gradually diminished and it is now normal. The pulse-rate has continued to be rapid. The friction-rub has disappeared and the area of cardiac flatness has decreased in size. The signs of compression of the left lower lobe have disappeared.

As you see, the patient had on admission this high, irregular fever, which has gradually come down to normal. His pulse rate too has fallen. There is still a wide area of cardiac flatness, but there has never been an extensive effusion. You see here in the *x*-ray that the heart shadow has not the characteristic triangular form extending up to the neck which is an indication of pericardial effusion. The cardiohepatic angle is well preserved and when the effusion is small this angle is not always obliterated. To contrast with this picture we have here another of a patient who was in the hospital a year ago. You see this tremendous shadow filling up nearly all of the lower part of the chest and tapering up to the sternal notch. This is the largest pericardial effusion I have ever seen. In the instance of the patient we show today there was never any occasion to consider aspirating the pericardium. The heart action was not embarrassed by the small amount of fluid present. Although it has the appearance of being very simple, you must not believe that

it is always easy to drain the pericardium, even though a large effusion be present. The patient with this extreme effusion was aspirated twice, and on each occasion only about 500 c.c. could be withdrawn. You have seen the shaggy exudate on the pericardial surfaces in pericarditis, and it is very difficult to keep the lumen of the needle clear. I have seen other cases where tapping was unsuccessful, and the suggestion has been made that it would be well in such cases to introduce a small, soft-rubber catheter into the pericardial sac. Large pericardial effusions requiring aspiration do not occur frequently. But it is important that you be familiar with the details of the operation. *A propos* of an interesting case, Dr. Thayer discusses the matter fully in an article that appeared in the Bulletin a few years ago.

The diagnosis in this instance is so obvious that it requires no discussion. I have already said that tuberculous peritonitis is much less common than tuberculous pleurisy, and tuberculous pericarditis is much less common than peritonitis. The cause of this disproportion depends, no doubt, upon the different incidence of tuberculous disease in the organs which these serous sacs cover or lie contiguous to. Tuberculosis affects the lungs more commonly than any other organ; tuberculosis of the liver, spleen, and intestines occurs much less frequently; tuberculosis of the heart is a great rarity. I do not mean to imply that tuberculosis of a serous surface is always directly spread from an underlying lesion in an organ. We are, unfortunately, very poorly informed about the mode of invasion in serous membrane tuberculosis. In the peritoneum it may be spread from a tuberculous lesion in the intestines, in the pelvis, or in the abdominal lymph-glands. When such a direct spread cannot be demonstrated, we must assume invasion through the lymph channels or through the blood-stream. The lymph currents flow always away from the serous surface, and to make this route plausible we must assume retrograde infection, always an unsatisfactory assumption. Nor does the blood-stream offer an easier explanation. It is difficult to see how the vessels to the peritoneum alone become infected, and in instances where the disease is local and not a part of a generalized tuberculosis,

the infection of the blood-stream could not occur at a distant point. In tuberculous pericarditis the infection comes nearly always from a contiguous mediastinal gland. A very remarkable case was demonstrated last year in which tuberculosis in the mediastinal glands had involved the pericardium and the heart muscle, and a caseous focus had finally ruptured directly into the cavity of the heart.

Tuberculous pericarditis stands between pleurisy and peritonitis as regards prognosis. It is a more serious manifestation than pleurisy, less serious than peritonitis.

We come now to view serous membrane tuberculosis as one manifestation of the course of tuberculous infection. Tubercle bacilli, after they enter the body, are carried rapidly to the lymph-glands. Dr. Krause has shown, in an interesting series of experiments, that it is almost impossible to directly infect the lungs. Provided a thorough emulsion of tubercle bacilli be used, large numbers may be injected directly into the ear vein and none can be recovered from the lungs. They must, of course, lodge there, but with great rapidity they are transported to the bronchial lymph-nodes. Most of them are filtered out in this way, but the filter is by no means perfect. Dr. Krause has further shown that if guinea-pigs be inoculated into the groin, the inguinal glands quickly become infected, but a few days after the inoculation the bronchial glands are also infected. Organisms must enter the blood-stream, be carried to the lungs, and from there be transferred to the bronchial glands. If infection be slight, perhaps only the regional glands are infected, but in many instances a wide glandular infection occurs. After such a primary infection has occurred the behavior of the animal toward subsequent infections is promptly altered. All of the cells of the body become so sensitive to the tubercle bacillus and its products that they react violently when brought in contact with it. Koch observed this reaction and describes it clearly. I will read you his description:

"When one inoculates a healthy guinea-pig with a pure culture of tubercle bacilli the wound, as a rule, closes and in the first days seems to heal. However, in from ten to fourteen

days a hard nodule appears which soon breaks down, leaving an ulcer that persists to the time of the death of the animal. There is quite a different sequence of events when a tuberculous guinea-pig is inoculated. For this experiment animals are best suited that have been successfully infected four to six weeks previously. In such an animal the inoculation wound likewise promptly unites. However, no nodule forms, but on the next or second day after a peculiar change occurs. The point of inoculation and the tissues, about over an area of from 0.1 to 1. cm. in diameter, grow hard and take on a dark discoloration. Observation on subsequent days makes it more and more apparent that the altered skin is necrotic. It is finally cast off and a shallow ulceration remains which usually heals quickly and permanently without the neighboring lymph-glands becoming infected."

This reaction is now generally described as a hypersensitive reaction, and it is important to be familiar with its manifestations, for without such knowledge it is impossible to have a clear understanding of the clinical manifestations of tuberculosis.

An animal infected with tuberculosis rapidly acquires an altered power of reaction toward subsequent injections of tubercle bacilli. This altered reactivity is exhibited in different ways, depending upon the manner and the intensity of the reinfection:

1. If a large number of tubercle bacilli are injected, the animal dies in a few hours with symptoms of a profound intoxication.

2. If the dose be small, there is a prompt reaction about the site of injection which destroys the tubercle bacilli and prevents infection even of the regional lymph-glands.

3. If the size of the dose be larger than that which the animal is able to resist, but not large enough to liberate acute fatal intoxication, infection does occur, but the resulting lesions are chronic and slowly progressing as compared with those produced by the same dose in normal controls.

These results, so contradictory at first sight, are easily

reconcilable. It is reasonably probable that the mechanism, whatever it may be, which causes the immediate toxic reaction on reinfection is the same upon which the animal withstanding this reaction depends for its complete protection. How analogous these phenomena are to the general principles of anaphylaxis is at once apparent. The animals have by one infection been rendered hypersensitive to subsequent contact. This hypersensitiveness is a valuable protective asset, but if the reinfecting dose be large the animal succumbs with the symptoms of an acute intoxication.

Dr. Trudeau, in his experiments on immunity to tuberculosis, has found that the more virulent the organism, the higher is the degree of protection against reinfection. In his experiments, histologic examination of the organs showed a remarkable difference in the type of reaction. The tuberculous animals showed upon reinfection an early and violent inflammatory reaction about the bacilli, which was followed in many cases by disintegration of the bacilli and subsequent absorption of the exudate. In normal animals no such immediate inflammatory reaction occurs about the injected tubercle bacilli. Tubercles slowly form and then go on to caseation.

Infection of the serous sacs shows the same relations that have been described for the general infection of animals. In uninfected animals little or no reaction is occasioned by the injection of tubercle bacilli, and the organisms are rapidly transported to the neighboring lymph-glands. In infected animals an immediate and violent inflammatory reaction is produced, followed by extensive exudation. Masses of shaggy exudate cover the surface and serous fluid accumulates in the sac.

Serous membrane tuberculosis is, therefore, a local hypersensitive reaction to infection in an already infected person. Only on this basis can we explain the acute onset of symptoms, the fibrous exudate, and the serous effusion. It illustrates also how a relatively small infection may cause a wide-spread and violent reaction. It is possible that a subserous focus of disease may cause serositis without tubercle bacilli actually reaching the surface. The infrequency with which tubercle bacilli can be

demonstrated in the serous effusion of serous membrane tuberculosis lends some support to such a possibility.

I come finally to the last consideration, that is, to view tuberculous peritonitis and tuberculous pericarditis as a part of disease of the large serous sacs. I have already commented upon the great frequency with which more than one serous cavity is affected. This combination is often enough observed clinically; anatomically it is still more striking. Some years ago I analyzed the autopsy records of 35 cases of tuberculous peritonitis and discovered these remarkable relations:

Twelve cases had an associated peritoneal and pleural tuberculosis and 9 more showed pleural adhesions without demonstrable tubercles.

In 2 cases there was an associated peritoneal and pericardial tuberculosis, and in 1 more an adherent pericardium without demonstrable tubercles.

One case showed tuberculosis of all three serous membranes.

Two cases had adherent pleuræ and pericardium without demonstrable tubercles.

In 1 case there was peritoneal and pleural tuberculosis with adherent pericardium in which no tubercles were found.

Direct channels of communication between the serous cavities have not been demonstrated, but our clinical experience inclines us to assume their presence.

Tuberculous polyserositis has a close relation to an interesting group of cases exhibiting a chronic inflammation of one or more of the serous sacs. These cases are described in the literature as Zuckergussleber (Curschmann), pericarditic pseudocirrhosis (Pick), polyserositis, and polyorrhomenitis. They are characterized by—

1. A chronic inflammation with the formation of a dense, thick, fibrous exudate.
2. Transient attacks of acute inflammation.
3. The formation of abundant effusions.
4. The absence of bacteria and of typical histologic structure in the fibrous exudate.
5. The striking chronicity of the condition.

The relation of this type of chronic inflammation of the serous membranes to tuberculosis has been widely discussed.

Some cases clinically identical with chronic polyorrhomenitis are proved at autopsy to be tuberculous; some cases not definitely tuberculous harbor foci of tuberculosis in the organs or glands; in the majority of cases there is no distinct evidnce of tuberculous disease. This disease and its relation to tuberculosis is fully discussed by Kelly and by Nicolls.

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AURICULAR FIBRILLATION

S. R., age forty-five; female; white; widow.

Entered the hospital November 14, 1918, complaining of shortness of breath and swelling of legs. The patient has been under observation in the Out-patient Department since 1909. She has had three previous admissions to the hospital, the first in April, 1916, the second in November, 1916, the third in October, 1917. A diagnosis of mitral stenosis and insufficiency was made when she came to the Out-patient Department in July, 1909. This diagnosis has been confirmed on all subsequent admissions to the hospital. When she was in the hospital in April, 1915, the pulse was irregular and the electrocardiographic study demonstrated typical auricular fibrillation. On the second admission in November, 1916, the Wassermann reaction was positive. On each occasion the patient has entered the hospital with the characteristic symptoms of myocardial insufficiency. On her first admission it was also noted that the pupils were irregular and that they failed to react to light.

Family History.—Shows nothing of importance.

Past History.—Numerous attacks of tonsillitis in childhood, but no history of rheumatism. Panhysterectomy performed in 1905 for pelvic abscess. The patient has had shortness of breath on exertion for at least twenty years. For ten years there has been cough, with occasional bloody expectoration. Some swelling of the legs during the past year.

Present Illness.—Five weeks before admission to the hospital she began to have marked palpitation of the heart, and shortness of breath again became extreme. Two weeks before, her legs began to swell and she experienced precordial distress.

Physical Examination.—Temperature 98.6° F. Pulse 96. Respirations 36. Blood-pressure 138/90. Patient is poorly developed and emaciated; marked dyspnea and orthopnea. Legs moderately edematous. Lips and cheeks cyanosed. Has con-

siderable cough, with mucoid expectoration. Typical Argyll Robertson pupils, a little irregular. Dental caries and oral sepsis.

Lungs: Fluid in the right pleural cavity; numerous moist râles.

Heart: Extremely enlarged, the area of superficial dulness measuring 6 cm. to the right and 17½ cm. to the left of the median line. At the apex, a rough diastolic murmur, snapping first sound and loud, blowing systolic murmur. Second pulmonic sound accentuated. Pulse totally irregular—small volume. Ventricular venous pulse. *Abdomen:* Distended. Slight hernia in scar of operation wound. Moderate ascites. Liver extends to the umbilicus. Spleen not enlarged. Deep reflexes normally active.

Laboratory Notes.—Blood: Hb. 92 per cent. R. B. C. 4,664,000. W. B. C. 5720. Differential count essentially normal. *Urine* contains a moderate amount of albumin and numerous hyaline and granular casts. *Wassermann* reaction negative.

Electrocardiographic Report (November 18, 1918).—Rate 80. Rhythm totally irregular. No P-waves present. T-wave negative in Lead 2. Diagnosis: Auricular fibrillation; right ventricular preponderance.

Course in Hospital.—During patient's stay in the hospital her symptoms have improved.

Diagnosis.—Chronic rheumatic endocarditis; mitral stenosis; auricular fibrillation; myocardial insufficiency; syphilis; cerebrospinal syphilis.

F. C., age thirty-two; male; colored; single.

Came into the hospital November 7, 1918, complaining of shortness of breath, cough, and abdominal discomfort. The patient had been in the hospital from August 3, 1918, to September 5, 1918. At that admission the diagnosis of chronic endocarditis, mitral insufficiency, and myocardial insufficiency was made. On the first admission the patient entered the hospital for shortness of breath. The family history was essentially negative. The patient stated that his general health had been

good up to the onset of the symptoms that brought him to the hospital. There was a definite history of rheumatic fever in 1913. In the winter of 1917 he had an attack of pleurisy. Four years previously he had had a chancre, and he received treatment for only three weeks. After leaving the hospital he was admitted again on October 1, 1918, and discharged on October 27th. On this occasion he came in again for shortness of breath. On both admissions the patient responded satisfactorily to treatment and was discharged from the hospital improved. After his discharge on October 27th the patient was able to walk several blocks without discomfort.

Present Illness.—On November 1st he caught cold and soon after became very short of breath and had abdominal discomfort. Cough developed and he had mucoserous expectoration. His throat has been a little sore. The patient thinks he has had no fever. The shortness of breath became so marked that he has been obliged to sit propped up in bed. His legs have become swollen, but not so markedly as on the previous admissions. His appetite has been very poor and he has vomited frequently. The patient has had abdominal discomfort, described as "heaviness," and a dull pain in the abdomen, particularly when he gets up. He has been sleeping poorly at night.

Physical Examination.—Temperature 98.6° F. Pulse 108. Respirations 26. Blood-pressure 158/112. Fairly well nourished. Marked dyspnea and orthopnea. Slight pitting of legs and ankles. Examination of the head showed no noteworthy abnormality except the dental caries and oral sepsis. *Lungs:* Showed only the signs of pulmonary congestion, with a small amount of fluid at the right base. *Heart:* Was enlarged, the area of relative cardiac dulness measuring 5 cm. to the right and 11 cm. to the left of the median line. Rhythm regular, except for an occasional extrasystole. A loud, blowing systolic murmur at the apex and markedly accentuated second pulmonic sound. *Abdomen:* Showed a small amount of ascites and a large, tender liver.

Laboratory Notes.—Blood: Hb. 70 per cent. R. B. C. 5,600,000. W. B. C. 7680. Differential count essentially nor-

mal. The Wassermann reaction, which had been positive on the two previous admissions, was doubtfully positive. *Urine:* Contained a moderate amount of albumin and a small number of casts.

Course in Hospital.—Under digitalis therapy the patient's condition improved. The pulse-rate, which on admission was 120, fell to 54. A definite bigeminal rhythm developed, which was broken by irregular groups of extrasystoles. On November 9th an electrocardiographic study showed a complete auriculo-ventricular dissociation, with varying auricular and ventricular rhythm, and an occasional ventricular response. When digitalis was stopped, the ventricular rate remained low, but the auricles began to fibrillate. On November 13th the electrocardiographic study showed: "Rate 60 per minute. Rhythm totally irregular. No P-waves. T-wave inverted and almost imperceptible in all three leads." As the pulse-rate increased the rhythm again became regular. At the same time the patient, whose general condition had improved, became very short of breath; the liver became greatly swollen and pulsated. Electrocardiographic report on November 20th reads as follows: "Rate 120. Rhythm regular. P-R. interval 0.14 second. Ventricular deflection quadriphasic in Lead III and of low voltage. T-wave in Lead III practically iso-electric. Slight left ventricular preponderance." On November 21st the patient received 0.5 mg. of strophanthin, and the same dose on the two succeeding days. The pulse-rate fell to 65. The patient became comfortable and the swollen liver gradually went down to normal size. The rhythm remained regular except for occasional extrasystoles. On November 27th the following electrocardiographic report was made: "Rate 58. Rhythm regular. P-R. interval 0.2 second. T-waves all positive." Since that date the patient's condition has remained unchanged.

E. K., age fifty-four; male; white; married.

The patient entered the hospital on November 7, 1918, complaining of heart trouble. He has had three previous admissions to the hospital. The first admission was in August, 1917, when

a diagnosis of myocardial insufficiency, auricular fibrillation, and colloid goiter was made. The patient left the hospital on September 14, 1917, improved. He was admitted to the hospital again for shortness of breath on November 30, 1917, when the same diagnosis was made. After leaving the hospital he was better for a while, but in June, 1918, the symptoms recurred, and he was admitted again, leaving the hospital improved on July 13th.

Family History.—Contains nothing of importance.

Past History.—The patient has always been strong and healthy up to onset of present illness. He has had a goiter for at least forty years. Although this has grown to a considerable size, it has never given him any discomfort.

Present Illness.—The patient's illness began in August, 1917, when he was obliged to stop work on account of shortness of breath, weakness, and swelling of the legs. These symptoms have recurred persistently since then. After the patient's discharge from the hospital on July 13, 1918, he returned to his work as a policeman and was well until October 31st, when severe shortness of breath again came on. He was obliged to stop work on November 4th, and since then has had marked dyspnea and orthopnea.

Physical Examination.—Temperature 98° F. Pulse 84. Respirations 34. Blood-pressure 158/104. The patient is fairly well nourished. Marked dyspnea and orthopnea. Edema of legs and the dependent parts. Lips cyanotic. The examination of the head shows nothing important except oral sepsis. The thyroid is greatly enlarged, the right lobe larger than the left; the whole gland is very irregular and firm. *Lungs:* Show no important abnormality except for the presence of fluid in the right pleural cavity. *Heart:* Is enlarged, the area of cardiac dulness extending 5 cm. to right and 16 cm. to left of median line. No murmurs. Aortic second sound somewhat accentuated. The pulse is totally irregular; there is a slight pulse deficit; the radials are slightly thickened. *Abdomen:* Liver a little below costal margin.

Laboratory Findings.—Examination of the blood showed no

important abnormality. The Wassermann reaction was negative. Phthalein test: 79 per cent. excretion in two hours. Adrenalin test was quite negative.

Electrocardiographic Report (November 11, 1918).—Rate 80. Rhythm irregular. P-wave absent. One right ventricular premature beat. T-wave inverted and ventricular complex diphasic in all three leads. Low voltage in all three leads, especially in Leads I and II, with notching of the initial deflection. Impression: Auricular fibrillation and ventricular extrasystole.

Course in Hospital.—During his stay in the hospital the patient has shown marked improvement under digitalis therapy. The shortness of breath and the edema have completely disappeared.

F. W., age fifty-one; male; white; married.

The patient entered the hospital November 16, 1918, complaining of shortness of breath and swelling of abdomen and legs.

Family History.—Essentially negative.

Past History.—Had been a healthy man up to onset of the present illness. There is a history of morning cough for the past ten or fifteen years, and cough at night as well for the past six or seven years. He has used tobacco and alcohol moderately; otherwise nothing noteworthy in the past history.

Present Illness.—In the summer of 1916 the patient began to have shortness of breath on exertion and indefinite pain in the abdomen. His legs and body became swollen. Under treatment his condition improved. At the end of December, 1916, he had another attack of shortness of breath, abdominal pain, and edema. Ever since then he has had shortness of breath and some swelling of the legs, which, however, has varied a good deal in intensity from time to time. One year ago he was confined to bed for seven weeks on account of these symptoms. Since then he has been obliged to spend two or three weeks in bed on different occasions. He has been on a low diet for the past two years, and he attributes his weakness and loss of weight to this. He has lost about 40 pounds. Nycturia three to four times during the past year. He has become very nervous and irritable.

He sleeps poorly and often has marked shortness of breath when he is in bed. Three weeks ago the shortness of breath and swelling of the legs became more severe than they had ever been before, and since then he has remained in bed.

Physical Examination.—Temperature 100° F. Pulse 82. Respirations 34. Blood-pressure 184/110. The patient is well nourished. Marked dyspnea and orthopnea. General anasarca. Examination of the head shows nothing important except a few retinal hemorrhages and oral sepsis. The chest is broad and deep, with moderate fixation. *Lungs:* Show a moderate grade of emphysema and numerous moist râles over both lower lobes. *Heart:* Is enlarged, the area of relative cardiac dulness measuring 5 cm. to the right and 16 cm. to left of median line. Slight dulness over manubrium. A loud systolic murmur at the apex. The aortic second is not accentuated. The pulse, though slow, is totally irregular. No pulse deficit—equal at the two wrists. Radials and brachials thickened. *Abdomen:* Greatly distended with fluid.

Laboratory Findings.—Examination of the blood showed no important abnormality. The Wassermann reaction was positive. Phthalein: 51 per cent in two hours. The urine showed a moderate amount of albumin and hyaline and granular casts.

Course in Hospital.—The abdomen was tapped on November 22d, when the liver edge could be felt $4\frac{1}{2}$ cm. below the costal margin. The organ was very firm, but regular. The spleen was not felt.

Electrocardiographic Report (November 18th).—"Rate 80. Rhythm totally irregular. P-waves seen only clearly in Lead II. Longest P-R. interval measures 0.3 second in Lead I. Left ventricular preponderance. T-waves inverted in all leads." Under digitalis therapy the patient's condition has improved. He is now comfortable and the edema has disappeared. The ascites persists.

Diagnosis.—Hypertension, arteriosclerosis, chronic nephritis, syphilis, cirrhosis of the liver, myocardial insufficiency, and auricular fibrillation.

These 4 patients presenting different clinical pictures have all certain features in common. For instance, they all show the clinical manifestations of myocardial insufficiency. Likewise, they all have an irregular pulse. It is this irregular pulse so similar in type in the 4 patients with clinical manifestations in other respects so dissimilar that I wish to consider especially this morning.

Here is a patient with mitral stenosis who has had symptoms on the part of the heart for over twenty years; for nine or ten years her pulse has shown always, at least whenever she has been examined, the same kind of irregularity that is present this morning.

As you feel the pulse you notice at once that the beats come at irregular intervals and are of varying amplitude. The pulse is slow—about 70 beats to the minute—and although one does not get at the first touch the sensation of extreme irregularity that one gets when under the same conditions the pulse beats rapidly, still, one has a better opportunity to study the condition in detail. If the pulse is felt carefully, you note that no two beats are separated by the same interval; hardly any two beats have the same force. As you listen over the heart and feel the pulse, you notice that some contractions are too feeble to be registered at the wrist. If you put on the blood-pressure cuff, the variation in force of the beats is still more strikingly shown.

As you look at the vein in the neck, instead of the double undulation and the systolic emptying of the veins ordinarily seen, there is but a single pulsation, and this comes synchronously with ventricular systole.

The second patient has mitral insufficiency, the result of rheumatic endocarditis. The pulse at present is perfectly regular, but you have heard the history.

While the patient was under observation in the ward the heart action suddenly became very irregular. At the end of about twenty-four hours the normal rhythm returned. Shortly after the onset of the irregularity breathlessness increased, the liver rapidly swelled and became a pulsating mass, again rapidly decreasing in size after the irregularity ceased. In this instance

the irregularity of the heart action seems to have been the immediate cause of the break in cardiac compensation.

The next patient has an enlarged thyroid, and associated with it a greatly enlarged heart. Although a systolic murmur is heard, there is the best of grounds for believing that he has no valvular lesion. I cannot stop to consider the relation between the enlarged thyroid and the heart condition, but there is a mass of clinical observations that justify our belief that there is a very intimate relation between the two. In this patient the myocardial insufficiency in the absence of valvular disease and hypertension and pulmonary disease is certainly the result of extensive myocardial disease. When the patient first came to the hospital about eighteen months ago his heart was very rapid and extremely irregular. If I remember clearly the history of this first admission, the rapid, irregular heart action and the symptoms of myocardial insufficiency came on together. Under treatment the pulse quieted down, the irregularity became less marked, and the symptoms of myocardial insufficiency disappeared. Since then the pulse has remained slow, but quite irregular, the condition that now persists.

Finally, in the fourth case with a complicated clinical picture which we will not stop to consider in detail, we again find this same peculiar and interesting irregularity of the heart action. The heart is beating slowly, but, as in the other cases, the beats come at irregular intervals and are of unequal force. This patient has hypertension, and no doubt the hypertension together with myocardial changes explains the myocardial insufficiency. Which of these two factors plays the more important part it is impossible to say.

To all of us older physicians who have practised medicine for twenty years or more this remarkable irregular heart action holds a fascinating interest. We have lived through the period when the nature and meaning of this phenomenon were totally obscure; then through the period when in spite of better methods of observation it still eluded discovery although shrewd surmises were being made about it; and finally, through the crowning period, when with still better methods the mystery was solved.

The story of the development of our knowledge of this form of cardiac irregularity is one of the most interesting and useful chapters in modern medicine. I shall tell you the story briefly.

I remember seeing these cases as a student and an intern. No special comment was made upon them except the platitudinous note that the pulse was irregular in force and rhythm. Not infrequently, however, the clinical picture was more dramatic and called for stronger terms. Patients came into the hospital breathless, with swollen legs and enlarged, tender liver; the heart beat tumultuously without rhyme or rhythm in almost a convulsive frenzy. The condition was then dignified with the term "delirium cordis." It was noticed that this delirium cordis occurred with noteworthy frequency in mitral stenosis and it was often referred to as the mitral pulse. When it occurred in mitral stenosis it was clearly noted that certain interesting changes occurred in the heart sounds. The presystolic murmur became changed in time and character and frequently disappeared altogether. The booming first sound, however, persisted, and on the character of this sound and the associated clinical findings adepts would confidently make a diagnosis of mitral stenosis, to the surprise and admiration of tyros. One more clinical symptom was frequently observed in these patients. The veins in the neck, which often stood out prominently, failed to show the normal venous undulation; in its place a prominent systolic pulsation was seen which was attributed to tricuspid insufficiency.

In those days the only graphic records made were of the radial pulse. I doubt if any of you has ever seen a Dudgeon syphmograph, but it was a familiar instrument on the wards at that time. The radial tracing showed just what could be felt at the wrist, and I remember that we were more interested in a scrutiny of the character of the pulse-wave than we were in fruitlessly trying to analyze an obvious irregularity.

In 1902 a very remarkable book appeared entitled "Study of the Pulse," by Mackenzie. You all no doubt know that Mackenzie was at that time a general practitioner in a relatively small

city. He has since become one of the foremost clinical authorities upon the heart.

Mackenzie before 1890 began using jugular as well as radial tracings in the study of the heart's action. Such observations had been made previously by Riegel, for instance, but he was the first to use the method systematically.

Before the publication of his book in 1902 definite progress had been made in the recognition of cardiac irregularities. Extrasystoles were fully understood, and nearly all the important facts concerning heart-block had been worked out. However, this curious irregularity which we are now discussing remained entirely unexplained. Let me read you what Mackenzie says of his own observations:

"My attention was first directed to this condition as a separate and definite entity about 1890. I had been endeavoring to discriminate between the different forms of irregular heart action, and it occurred to me to employ the jugular pulse as an aid. By this means I was able to separate the great majority of irregularities into definite groups, according to the mechanism of their production, as revealed by simultaneous records of the jugular and radial pulses. There was one group which showed a distinct difference from all others, by the presence of the ventricular form of the venous pulse. I was at a loss to understand the nature of the heart's action in these cases; and as I found them very frequently among people with a history of rheumatism, I determined to watch individual cases with rheumatic hearts, to see when this irregularity arose, and when the auricular venous pulse changed to the ventricular. The individual recorded as Case 48 came under my care in 1880, suffering from an attack of rheumatic fever. I examined her at intervals until her death in 1898. Up to 1897 her heart was regular, except for occasional ventricular extrasystoles. Her jugular and liver pulses were always of the auricular form. There was a well-marked presystolic murmur. She became very ill in 1897, with a rapid and irregular heart. When the heart slowed down after a partial recovery, I found that the jugular and liver pulses were of the ventricular form, that the presystolic murmur had disappeared,

and that the heart was irregular; in other words, all evidences of auricular activity had disappeared. From this date onward I was able to confirm these observations, and add to them other cases which showed waves due to the auricle, in jugular and apex tracings before the heart became irregular, and their disappearance when the heart became irregular. Thus, I established that all the positive evidences of auricular activity capable of being revealed by clinical methods showed the cessation of auricular action with the onset of this irregularity. For many years I speculated as to the cause of auricular fibrillation. As the auricle was found distended and thin-walled at the postmortem examination, I came to the conclusion that the disappearance of the signs of auricular systole was due to the auricle having become distended, atrophied, and paralyzed."

What a remarkable statement that is, and what a simple and still penetrating deduction from his observations. Had Mackenzie only stopped there! Unfortunately, further observations led him off from this simple and sound conclusion and landed him at last in gross error. Let me continue with Mackenzie's own words:

"Shortly after this was published I had a series of cases, some of which I had watched for years, and at the postmortem examinations the auricles were not thinned, but were hypertrophied. With this fact before me I saw that my previous explanation could not be correct; for the fact that the auricles were hypertrophied indicated that they must have contracted during the years that I had watched them, and when there had been an absence of all signs of auricular activity. As it was clear that the auricles could not have contracted during the normal period—that is to say, immediately before ventricular systole —the only alternative I could see was that they contracted during ventricular systole. As, in the meantime, I had studied several hundreds of cases and had seen this condition start under a variety of circumstances, particularly in individuals with frequent extrasystoles, I put forward the view that ventricles and auricles contracted together, and assumed that the stimulus for contraction arose in some place that affected auricles and

ventricles simultaneously. As at this time I could not conceive of any other possibility to explain the facts, I suggested that the stimulus for contraction arose in the auriculoventricular node; and I called the condition 'nodal rhythm.' "

While Mackenzie was pursuing his work in England, clinicians in other countries were busy with similar methods of investigation. I may mention particularly Wenckebach in Holland and Herring in Germany. All other known forms of cardiac irregularity were soon accurately analyzed and their mechanism understood, but the most interesting and striking of all the irregularities remained unexplained. It refused to fit itself into any of the known categories; all one could say of it was that it was an unanalyzable irregularity which when once begun nearly always persisted. Almost in despair, clinicians called it the irregularly irregular pulse; the absolutely irregular pulse; the pulsus irregularis perpetuus.

In 1906 a fresh shaft of light was shot into the obscurity, this time by a laboratory worker. Cushny was at that time Professor of Pharmacology at Ann Arbor, and he published his observations in conjunction with Edmunds. The article is so important that I shall read a few short excerpts from it:

"The following case of marked irregularity of the heart occurred in the service of Dr. Peterson, Professor of Gynecology and Obstetrics in the University of Michigan. Careful examination of the heart was made and a number of sphygmographic tracings were obtained. Unfortunately, at that time we were not acquainted with Mackenzie's methods of taking the venous and liver pulses, and failed to take advantage of this most valuable method of analyzing cardiac irregularity. The case is of considerable interest, however, and the light which seems to be thrown on it by our experience of irregularity in animal experiments encourages us to put it on record. . . . In the course of the long series of experiments and deomonstrations on the dog's heart carried out in the pharmacological laboratory of the University of Michigan during the last seven years it has happened occasionally that on opening the chest the heart was found to be beating very rapidly and irregularly. Doubtless other

workers in this field may have had similar unfortunate experiences, but we are unaware of any recorded cases. Our dogs were anesthetized with morphin, 0.2 to 0.3 gram hypodermically, and chloretone administered by the stomach-tube. The operation consisted in performing tracheotomy, prolonging the median incision to the lower end of the sternum, sawing through the sternum along its whole length, and hooking the two sides of the chest apart, thus exposing the pericardium, which was opened. The myocardiograph was then applied to the ventricle and auricle and tracings taken on a kymograph with smoked paper. The anesthesia was invariably deep enough to prevent any manifestation of pain and the eyelid reflex was absent before the incision was made. Sometimes, however, spontaneous respiratory movements returned while the sternum was being cut through, or if these were present before, they became quickened and deepened. It was soon noted that when this change occurred the tendency to cardiac irregularity was much greater than in those experiments in which more profound anesthesia had been induced. Attempts were made to record the changes in the pulse during the operation, but in the experiments in which this was done the irregularity was not developed. In several cases, however, it was noted that the heart rhythm was normal before and during the first part of the operation, but that when respiratory movements were induced by cutting through the sternum, the pulse, which had previously been of the usual slow vagus type seen in the dog, suddenly became accelerated and irregular. On examination of the heart in these cases, before the apparatus was applied to it, the ventricles were found in rapid, irregular movement; the relaxation was often very imperfect between three or four successive contractions, and then more complete for one or two beats. The impression was given that the ventricles were responding to a series of very rapid impulses which prevented their diastole, and that they could only relax when their irritability was reduced by fatigue, and then the more complete diastole followed. The auricles were widely dilated and no systole occurred in them; they were not wholly paralyzed and inactive, however, for on close inspection the fibers proved to

be in a stage of continual inco-ordinated contraction, each part of the auricle undergoing continuous fibrillary contraction independent of all other parts. The heart was, in fact, in the condition known to physiologists as auricular delirium, or fibrillary contraction in the auricle. . . . Of course, we cannot claim to have shown any connection between this type of irregularity in the dog's heart and that in the case described. At the same time there exist similarities between them, and the sudden arrest of the irregularity in each suggests a common cause; in the dog the site of the lesion is the central nervous system, and the history of the patient suggests that here also the irregularity was of central origin. We had hoped to have the opportunity of continuing the investigation in other cases of irregular heart, but as circumstances preclude our working further together, we have decided to put the imperfect investigation on record, in the hope that others may be interested in the suggestions made and may be able to prove or disprove its correctness."

Cushny carried these observations to a number of clinicians, among others to Mackenzie and Wenckebach. In his conversation with Cushny, Mackenzie showed tracings displaying small, rapid waves upon the venous pulse tracings, and both agreed that these might be the effects of auricular fibrillation. Indeed, Mackenzie the following year published such tracings, but he thought the condition transient and of little practical consequence. Certainly he failed to appreciate its real significance. Wenckebach replied to Mackenzie that such slight waves upon the venous pulse tracing were sometimes seen in tracings from hearts beating regularly. He was unwilling to allow that auricular fibrillation could be at the bottom of an irregularity lasting for years.

I must digress a moment to prepare you for the next development in this interesting story. Physiologists had long before noted that as muscular tissue contracts interesting electric changes occur in the muscle mass, namely, the contracting portion becomes electrically negative and currents flash through the muscle. In 1887 Waller was able to register the electric currents passing through the heart muscle by connecting the limbs

with a capillary electrometer. The instrument, however, was clumsy, and did not record accurately enough to be used as a clinical method. In 1903 Einthoven published his discovery of an unusually delicate galvanometer. By suspending a very delicate thread of silvered quartz in a magnetic field he was able to register deflections caused by the very faintest electric currents. In 1907 clinical reports of results obtained by using this instrument to register the heart action currents began to appear, and in 1909 Lewis, in England, and Rothberger and Winterberg, in Germany, by using this method established beyond question that the totally irregular heart action in man and experimental auricular fibrillation in dogs are identical.

We are indebted to instruments of precision and to all this painstaking work for the elucidation of the mechanism of the cardiac irregularity illustrated in these patients and which we now know to be due to auricular fibrillation. However, once this condition is fully understood, it is easily diagnosed by rough clinical methods. No physician can give as an excuse for lack of familiarity with auricluar fibrillation that an electrocardiograph is not available or that he is unable to devote sufficient time to obtain satisfactory polygraphic tracings. During the past five years we have made it a rule to diagnose all cardiac irregularities on the ward before electrocardiograms are taken. It is only occasionally that auricular fibrillation is missed. We meet auricular fibrillation in two forms: fibrillation with rapid pulse and fibrillation with slow pulse. With the onset of fibrillation the ventricle nearly always beats very rapidly and very irregularly; under treatment the ventricle slows down and the irregularity becomes much less marked. Fibrillation with rapid pulse is very easily recognized; when the ventricle beats slowly the pulse may on casual observation appear to be regular, but even under these conditions the diagnosis can be made in most instances by more careful observation. The conditions under which there is real difficulty in diagnosis are few. If there is complete auriculoventricular block, the fibrillating auricle has no influence over the ventricle. The pulse is slow and regular and the condition of the auricles would scarcely

be suspected. The diagnosis might possibly be made from the venous pulsation in the neck. The combination of auricular fibrillation and complete auriculoventricular block is so unusual that it will seldom tax our diagnostic skill. I have seen patients with a very irregular pulse from extrasystoles where fibrillation was suspected, but never one where an extrasystolic irregularity was mistaken for fibrillation. The great difficulty is when numerous extrasystoles occur in conjunction with auricular fibrillation. Under such circumstances I have seen the fibrillation overlooked. Auricular flutter with quickly varying ventricular response causing a very irregular pulse may easily be mistaken for fibrillation. The mistake is of little practical importance, but in many instances the two may be differentiated. In rare instances of gross sinus arhythmia the pulse may be so irregular that fibrillation is suggested. The effect of deep breathing, of exercise, and inspection of the venous pulse usually make the distinction easy.

The gross clinical signs by which we may recognize auricular fibrillation are these:

1. The pulse-beats are unequally spaced. When the ventricle beats rapidly this irregularity is so striking that the diagnosis is at once assured. When the ventricle beats slowly the irregularity is not so marked; indeed, occasionally the pulse seems to be regular. However, careful observation will soon convince one that the spacing between the beats is really unequal.

2. Unequal force of beats. This feature also varies with the rate of the ventricle, more obvious with fast than with slow rates. The unequal force of the beats is best appreciated when taking the blood-pressure. When the irregularity is great no true blood-pressure can be gotten; the systolic pressure may vary from 100 mm. Hg. to 200, and the diastolic pressure almost equally as widely. Taking the blood-pressure is of great help in the diagnosis of auricular fibrillation.

3. Pulse deficit. When the ventricle beats very irregularly some of the contractions are so feeble that they fail to register at the wrist. The pulse-rate, counted at the wrist,

therefore, is less than the ventricular rate counted over the heart. The pulse deficit is greater when the ventricle is beating rapidly than when it is beating slowly, and usually when the ventricle rate is below 60 no deficit occurs.

4. In fibrillation, the more rapid the pulse, the greater the irregularity. This is in marked contrast to extrasystolic and sinus arhythmias, where the converse is true. Exercise often brings out this distinction.

5. If a venous pulse can be made out in the neck, it is of the so-called ventricular type. That is, but a single large wave is observed which is systolic in time.

Clinically, auricular fibrillation is observed under the most varied conditions; it occurs in hearts already diseased, but also in hearts that present no evidence of any abnormality whatsoever aside from the fibrillation. It occurs with noteworthy frequency when the auricles are subjected to great distention, and is, therefore, commonly associated with mitral stenosis. But it occurs very often in connection with other valvular defects; in hearts hypertrophied from long-continued hypertension or from obstruction in the pulmonary circulation and in myocardial disease of every type. Of peculiar interest is the occurrence of fibrillation in hearts that present no other evidence of disease. The fibrillation comes on usually in paroxysms quite similar to the paroxysms of paroxysmal tachycardia. Such attacks may occur for many years, but in the end the fibrillation usually remains permanently. When hearts that are diseased begin to fibrillate, the fibrillation commonly persists during the remaining lifetime of the patient. This is peculiarly true in mitral stenosis. However, in conditions other than mitral stenosis, and particularly in myocardial disease, brief periods of fibrillation are commonly observed. I am becoming more and more impressed by the frequency with which transient periods of fibrillation occur in old people. After sixty, fibrillation may come on with varied upsets which have no direct connection with the heart. Gastro-intestinal disturbances frequently inaugurate it. As the symptoms of the acute disturbance pass off, fibrillation also disappears. I have seen 2 patients have such transient

attacks of fibrillation over a period of years and the fibrillation finally become permanent.

What I wish particularly to impress upon you is that you must look upon auricular fibrillation as an independent and distinct clinical entity; I mean independent of the particular cardiac disease with which it may happen to be associated, and as distinct from manifestations of myocardial insufficiency. Auricular fibrillation occurs frequently enough in otherwise normal hearts where it is the whole of the clinical picture, and when it occurs in hearts already diseased it adds something new and distinct to the clinical picture. Rather than to look upon it as one sign of a failing heart muscle, it were better to view it, which in fact it commonly is, as an important cause of myocardial insufficiency. A normal heart may stand auricular fibrillation without the slightest evidence of impaired function, but when the heart is handicapped by mechanical disadvantages, or its muscle is diseased, then the advent of fibrillation is quite commonly the added difficulty with which it cannot contend, and the usual symptoms of myocardial insufficiency are precipitated. How frequently does just that occur in mitral stenosis. With the onset of fibrillation the balance is upset and breathlessness and edema rapidly come on; under proper treatment the ventricles slow down, abortive, fruitless contractions are eliminated, the circulatory balance is re-established, and the symptoms of myocardial insufficiency disappear. The auricles continue to fibrillate with slow ventricular rate, and fibrillation may thus continue for many years.

I have emphasized the importance of regarding auricular fibrillation as a distinct clinical entity, and this emphasis is peculiarly warranted in speaking of treatment. Aside from any of the conditions with which it may be associated, fibrillation has a special, and I may almost say a specific, treatment. A normal heart subject to transient attacks of fibrillation may need no treatment; but if the paroxysm be prolonged the efficiency of the heart will suffer, as it nearly always does when fibrillation occurs in a diseased heart. We possess no remedy that will stop fibrillation and re-establish normal auricular movements, but we

can inhibit the fruitless agitation of the ventricles that fibrillation induces. It is in fibrillation that digitalis exercises its wonderful power. When the heart is brought under satisfactory digitalis influence the ventricular rate is slowed and with the slowing its action becomes more regular and the individual beats more effective. And digitalis must be given until this quieting effect is obtained or evidence of poisoning occurs. Only occasionally is a fibrillating heart refractory to digitalis. Time does not permit me to speak at length of the use of digitalis and its mode of action. I can only add one warning: Since the potency of digitalis preparations varies tremendously, it is futile to prescribe digitalis according to routine dosage. A teaspoonful of one infusion, for instance, may be as potent as a tablespoonful of another. Unfortunately, most preparations on the market are not standardized, and it is important that the physician should prescribe a preparation according to its effects and not according to text-book dosage. If an accurately standardized preparation is not obtainable, then the physician should use a single preparation with which he has become familiar. Its effect upon fibrillating hearts will be an index of its potency. You cannot write a prescription for tincture of digitalis for 6 patients if each patient has the prescription filled at a different druggist, and expect the same effect in all.

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CLINIC OF DR. ALLEN K. KRAUSE

JOHNS HOPKINS HOSPITAL

A CASE OF MULTIPLE TUBERCULOSIS IN CHILDHOOD

Full and Complete History of the Patient from His First Appearance at the Clinic in this Hospital Ten Years Previously; Onset of the Disease; the Influence of Trauma on the Production of Both Bone and Joint Tuberculosis; Site of First Infection; the Etiology of the Infection; Progression of Infection and Disease; Treatment; Full Discussion of the Use of Tuberculin; Sanatorium and Home Treatment; The Pirquet Skin Test; Prognosis.

January 15, 1919.

PRESENTATION OF THE CASE

THIS boy, born in the United States, of Italian parentage, is within a few weeks of his fourteenth birthday. He is 53 inches tall and weighs 70 pounds; yet well proportioned, with clear eye and good color, and every appearance of health. His physique, therefore, is that of a normal ten-year-old child. To account for his size we may at first think of his race, yet his brother whom you see here with him is almost two years younger, though a full half-head taller and weighing 93 pounds.

He has been under almost continuous observation at this hospital for ten years; and with this appearance of vigor and ruddiness before you let us review his story.

On January 27, 1909, he was brought to the dispensary, referred to the Dermatological Clinic, and from there at once transferred to the Surgical Clinic. He had a sore arm. Twenty-five days before he had fallen and struck his left arm and hand on the floor. Several days later the forearm became swollen and very painful. At about the same time his legs began to swell, and

this swelling persisted. Pain that was more severe at night had been constant in his arm and both legs. On the nineteenth day of his disease the swelling on his arm had been opened by a physician; and at the time of the patient's first visit to the dispensary this wound was still open and was discharging.

He was then just completing his third year. He was the fourth of five children. One brother and two sisters were living and in good health. One sister had died at the age of one year of what the mother said was "mumps." His father, forty years old, and his mother, thirty-four, were both well.

From birth he had always been healthy. He had escaped the infectious diseases of infancy and childhood. He had never before been ill.

He showed the rosary, sabre shins, and epiphyseal enlargements of rickets that had been recovered from. There was a small sinus over the left ulna at about the junction of the lower and middle thirds. The overlying skin was tender and inflamed, and evidently covered an abscess. Pressure in this region caused pus to exude. There was no bony thickening that could be felt. Over both tibiæ there was also slight tenderness and possibly slight swelling, though the latter was very difficult to make out.

The boy entered the hospital a week later, where on February 4th he was operated on. Through a small incision over the left ulna, at the site of the abscess, a small amount of pus was evacuated and the bone exposed. Though the sinus went down to the periosteum, no bare bone was felt. The ulna, explored to the marrow cavity, was found to be perfectly normal.

The patient left the hospital on February 13th with his wound granulating well, with no pain or discomfort, and with instructions to return in two days to the dispensary for dressings. After a few days, however, it was noticeable that he was not doing so well. He now began to complain more about his right leg; and whereas a month before it had been noted that "there was possibly slight swelling" over the tibiæ, though this "was very difficult to make out," on February 27th we find the record of "a smooth even swelling on the right shin bone, painful to pressure, apparently bone involvement, periostitis." By March 10th decided

fluctuation had developed, the tenderness was great, and the child looked quite ill. Meanwhile pus had again begun to exude from the unhealed operation wound in his left forearm.

He was therefore again sent into the hospital for operation on his right leg. On March 12th an incision was made over the most prominent part of the tibial swelling and the abscess explored. The abscess cavity was found to be inside the tibia. There was a small defect in the periosteum which was considerably roughened and thickened. At the same time the left arm was again gone into, when a pus cavity and a periosteal and bony defect of the radius was found. On March 22d the boy left the hospital with both wounds clean, the discharge slight, and granulations healthy and abundant.

From this time until the fall of 1909 the patient came regularly to the dispensary to have his wounds dressed. A diagnosis of syphilitic periostitis and epiphysitis was made, and, in addition to the local applications of boric ointment, a course of therapy with mercury and potassium iodid was instituted. Both of these measures continued for seven months, when on October 30, 1909, we have a note that the arm was healed, the ulcer on the leg about healed, and the patient discharged with a dry gauze dressing on his leg. Antisyphilitic treatment was, however, continued during the following winter, though up to this time there is no record of a Wassermann test having been performed.

On February 21, 1910, or thirteen months after he first came under observation, the child again returned to the Surgical Dispensary after an absence of two months, this time with a new complaint. He "comes in today with an enlarged left epitrochlear gland and also enlarged right inguinal glands, all quite tender and temperature over them elevated, although the skin is not red." He was given treatment with potassium iodid; and, since no change in his condition occurred, on March 5th he was transferred to the Pediatrics Clinic.

He here came under the observation of Professor Pirquet; and from the notes then made we begin to gather a few more pertinent details of history that are not to be found in the earlier records. We find that the sister who died of "mumps" at the

age of one year was a twin sister. The patient did have an infectious disease earlier in childhood. He had had measles when two years old. At the sites of his operation scars there is still some tenderness. For a month now his mother had noticed a swelling in his right groin; and for the last fifteen days a similar swelling on the inner side of his left elbow. His mouth is in poor condition. His throat and neck are negative. His heart and lungs are negative. His abdomen, however, is greatly distended, though symmetrically so. In the region of the descending colon there are masses to be felt. The edge of the liver is palpable 2 cm. below the costal margin. The spleen is not palpable. He was given a Pirquet skin test with old tuberculin and reacted strongly.

We have then in March, 1910, a five-year-old boy, born and brought up in a family in which there is no history of tuberculosis; whose twin sister died of "mumps" at the age of one year; who had rickets in infancy and measles at two years; who when almost four years old and in apparent health fell and injured his arm, as a consequence of which a lesion of his left ulna and radius developed. At the same time his legs are noticed to be swollen and an abscess of his right tibia gradually comes to light. Diagnosed as luetic epiphysitis, these bone abscesses are operated on, but heal with great sluggishness. After a year the lymph-nodes that drain the areas that first show disease begin to exhibit manifest involvement. And now a simple test—the Pirquet skin test—is applied, and it is found that the case is probably one of tuberculosis. Physical examination reveals no involvement of the neck or lungs; but does bring out unusual abdominal distention and palpable masses in the abdomen along the descending colon. The points to which we would call attention for the moment are (1) the development of a chronic bone lesion following injury, (2) the subsequent manifestation of another bone lesion at a remote focus, (3) the swelling of the legs that was recorded at first admission, but to which apparently no further attention was paid, (4) the involvement of neighboring lymph-nodes that took a full year to become manifest, (5) the hint thrown out that there is

some intra-abdominal trouble, (6) the normal pulmonary findings, and (7) the errors of omission in the handling of the case, such as incomplete history-taking and the failure to make early Wassermann and Pirquet tests. At any rate, at the end of a year we are practically certain that we have here in a young child manifest tuberculous adenitis of two widely separated lymph-nodes that has originated from unrecognized tuberculosis of bones with the bony involvement not yet completely healed (there is still tenderness); and there is a suggestion that all is not right in the abdomen.

From the Pediatrics Department the child was transferred to the Phipps Tuberculosis Dispensary; and here he became a patient on March 8, 1910. Under our observation during the nine years that have since elapsed we have had an unusual opportunity to note carefully the periodic arrest of disease, the halting march of manifest tuberculosis from point to point, the development and effects of other acute infections, the immediate and remote results of various therapeutic measures, the fluctuations of constitutional conditions, such as weight and temperature, and the variations of tolerance to tuberculin. During these first five years, from 1910 to 1915, we saw him from once to several times weekly; from 1915 to 1917, usually twice a month; and since January, 1918, at longer and more irregular intervals. This boy's history would furnish an almost complete epitome of the more common and characteristic manifestations of tuberculosis in early life; and from it many texts might be drawn and enlarged upon. It will be possible to take up with any attempt at detail only a few; most can be only alluded to or touched upon briefly. And before discussing any broader features of his case, we may rapidly sketch what has happened to him since he was known to be a case of tuberculosis.

His original history at the Tuberculosis Dispensary, taken on March 8, 1910, mentions that he has no cough, no pain, and no gastro-intestinal irregularities except for a very poor appetite. He has night-sweats, and for four months his feet have been swollen. His weight is 35 pounds, a deficiency of about 6 pounds for his age. His skin and mucous membranes are pale.

His temperature in the clinic is 99° F., his pulse 120, and his respirations 26. He comes complaining of large but painless swellings of the epitrochlear and inguinal glands and abdominal distention. More complete examination makes certain that his lungs are normal to percussion and auscultation, while his liver is palpable.

Tuberculin therapy was at once begun; and on March 12th he was given $\frac{1}{100000}$ mgm. old tuberculin subcutaneously. Two days later his back was slightly red and swollen and sore to the touch at the point of injection. Every few days he received tuberculin, and by March 29th had reached $\frac{4}{100000}$ mgm. Two days later the area about the point of injection is much swollen, very red, and very tender. In other words, at the very beginning of treatment he exhibits an extremely high degree of hypersensitiveness to tuberculin, reacting locally as he does to very minute doses. In the absence of constitutional symptoms tuberculin is, however, kept up, and on April 5th, following $\frac{4}{100000}$ mgm., there are evidences of a focal reaction. The inguinal glands are larger, red, and very painful and hard. The epitrochlear nodes are not tender, but are possibly larger. His abdomen does not seem so distended. By April 29th he is getting $\frac{1}{10000}$ mgm. O. T., and it is said that he is doing nicely and that the inguinal glands instead of feeling like one solid mass can be outlined. On May 10th he had pain in the abdomen, but otherwise he is doing well and looks better. Every now and then he reacts locally (at the site of the injection) to tuberculin. Nevertheless these injections are persisted in. Every third or fourth day they are given in gradually increasing dosage, until by May 27th they have reached $\frac{7}{10000}$ mgm.

Meanwhile during these three months from early March to the end of May his weight is fluctuating. Once on March 15th it reached 40 pounds. But the average reading is $36\frac{1}{2}$ to $37\frac{1}{2}$ pounds, and on May 27th it is recorded as $36\frac{3}{4}$ pounds.

On this day there is the following note: Has been having elevation of temperature at dispensary now for some time. Does not complain. Throat injected and tonsils enlarged. Cervical gland on left side also very large. The epitrochlear glands of

the left arm are about as usual; the inguinal on the right side, a little larger and harder. Scar on right leg doing nicely, but above this a red, inflamed area with a tendency to suppurate has appeared.

During the next ten days he continues to have symptoms and show signs of tonsillar inflammation, and on June 10th his tonsils and adenoids are removed. He makes a poor recovery from this operation, looks badly and eats little; and about the end of June it is noted that he is coughing a great deal. Nevertheless he receives his tuberculin regularly, and by July 12th is getting $\frac{16}{10000}$ mgm. His cough increases and he begins to vomit after coughing; and at this time it is definitely determined that he has whooping-cough. Tuberculin therapy is now interrupted for about six weeks, to be resumed on August 19th with a dose of $\frac{9}{10000}$ mgm.

He comes through his whooping-cough well. On August 19th his weight is 36 pounds, but he is looking well. On September 4th it is noted that his abdomen is large and that there is a suggestion of fluid. The right inguinal and left epitrochlear glands are still large. The upper end of the old scar on his right shin is red and swollen. Nevertheless, with the end of the summer and a return to cooler weather he begins to improve constitutionally. His tolerance to tuberculin gradually increases, and it is very rarely now that he shows any tendency to react at the site of injection. By November he reaches 40 pounds. All through December he maintains this weight; and increases until on January 7, 1911, we find a reading of $43\frac{1}{4}$. All through the winter and down to April 1, 1911, there is a monotonous though encouraging succession of notes, "Feels well," "Good," "All well"; and he has now reached 1 mgm. of old tuberculin. And on this day we find a record that indicates distinct improvement. On the right leg and left forearm there are now well-healed scars. In the right groin and left elbow conditions are satisfactory. The left axillary glands are just palpable. The abdomen is rather full, but is soft and relaxed. He has lost a bit in weight, which is now 41 pounds, a net gain of 6 pounds during the past year.

He continues to improve, and on April 28th we read that the left epitrochlear gland is not palpable and that the chest is clear. Throughout the spring and summer, however, his temperature shows a tendency to range between 99° and 100° F. and he makes practically no gain in weight. During July and August he weighs 39 or 40 pounds. He seems to feel well and takes his tuberculin well. By the end of September he is getting 100 mgm. without reaction. But during October and November he seems to be sick, coughs a good deal, and looks very pale, maintaining meanwhile an average weight of 43 pounds.

With colder weather he improves, gets up to 250 mgm. tuberculin by December, but on December 23d is found to be suffering with chicken-pox. After he recovers from this he is unusually well and goes through most of the year 1912 without untoward incident. His temperature at the clinic, however, is rarely below 99° F. and averages about 99.5° F. His weight increases a little and he finishes the summer weighing 46 pounds. On September 26, 1912, we find the first detailed note that has been made for almost a year and a half. He is frail, poorly nourished, and pale. Examination of his chest reveals slight impairment on the right side to the third rib in front, as well as slight impairment throughout the back. There are no râles, but the breath sounds are harsh. About the same conditions obtain on the left side. Here then after three and a half years are our first indications that something is going on in the lungs, though as yet there have been no pulmonary symptoms. It is also noted that the abdomen is distended and soft and that small, indefinite masses can be made out, "which may be tuberculous glands." The liver and spleen are not palpable.

He does uniformly well during the next winter. On March 1, 1913, over four years after first coming to the hospital, and three years since entering the Tuberculosis Dispensary, we find him weighing 48½ pounds, with no local trouble, and receiving 1000 mgm. of tuberculin. In three years, therefore, he has made a net gain of 13½ pounds, and is now 6 pounds under normal weight, just as he was then. But with the coming warmer weather he loses, and by the end of July is down to 46 pounds.

He is then sent to the country for three weeks, and comes back weighing 49⅝ pounds. A month later he is back again at 45½, but by November 1st he has again gone up to 48¼ pounds. Notwithstanding these rapid fluctuations, objectively he apparently remains the same. But as winter comes on he again begins to do unusually well. On February 28, 1914, he weighs 51½ pounds, when at the same time it is noted that he has a large painful gland, about the size of a hen's egg, in the left axilla that is without fluctuation.

You will remember that on April 1, 1911, we found a note that the left axillary glands were just palpable. Between then and now there has been no mention of these structures. Here then, three years after a probable enlargement of these nodes was first recorded, four years after the left epitrochlear nodes showed manifest disease, and six years after the first bone abscess of the left radius and ulna, we find an undoubted tuberculosis of the next chain of nodes, the axillaries, becoming manifest.

This axillary mass rapidly became soft, and on April 18th it was incised. Healing was slow and never complete. On November 28th the abscess was again opened and then dressed at intervals until on February 11, 1915, it was noted that there was a large confluent mass in the left axilla in which a small area of softening was apparent. In the mass were two partially healed scars which were incised last April and have been discharging intermittently since. The boy was then recommended for admission to the hospital for more radical operative interference.

During this period, between April, 1914, and February, 1915, while the axillary abscess was lazily developing, the patient gained very little ground, and from now on and through 1915 and 1916 his career was even more checkered than it had been before. Soon after the first signs of trouble in the axilla were noted his weight stopped increasing; and by August, 1914, it was as low as 47. Nevertheless he received his tuberculin regularly. During August and September he was given several repeated injections of 1000 mgm. at intervals of two weeks. On September 19th, following an injection, he felt giddy and sick at the

stomach and had loose bowels. At the same time he had considerable local pain and swelling. But then for a few months, during the time that the tuberculin was discontinued, he seemed to pick up a bit. Soon, however, the axillary condition became worse, and on February 12, 1915, he entered the surgical wards of the hospital for operation weighing about 50 pounds.

Here all the glands extending up to the apex of the axilla were dissected out. All were very large and tuberculous, and adherent to the vein. On March 13th he was discharged from the ward with his wound healing and his general condition good.

From now on he slowly lost ground. In a short time other symptoms developed; and early in April he began to have pain and vomiting after eating. He felt hungry, but could eat no solid food without vomiting and abdominal pain. His bowels also showed a tendency to looseness, and he had three or four stools a day. He was also losing weight more rapidly than had been usual for him at this time of the year. This condition kept up, and on May 11, 1915, he was again admitted to the wards. His abdomen was distended and bulging in the flanks, but there was no shifting dulness. The walls were soft. There was no tenderness on deep palpation. There is no note that at the time intra-abdominal masses were to be felt. The stools were of a diarrheic nature, but were not characteristic of any specific infection. A diagnosis of tuberculous peritonitis was now made for the first time. It was also noticed that there was an abscess of the rib just under the left clavicle, and that there were many palpable anterior cervical glands on the left side. On July 8th the abscess of the rib was opened. On July 28th the patient left the hospital with this wound almost healed and was sent to the country to convalesce in the care of the Social Service Department.

Here then we have the first plain evidences of peritonitis developing over six years after the child first came under observation, yet careful attention to his story brings out that during all this time there were indications that abdominal structures were involved. On his first admission the abdomen was noticably distended, an observation that appears every

now and then in the history. As far back as February, 1910, it was recorded in the Pediatrics Department that masses were to be made out along the descending colon. While he was in the hospital, with symptoms of peritonitis occupying the foreground, the boy also developed phlyctenular conjunctivitis. This, however, soon cleared up under appropriate local treatment.

On September 10, 1915, the boy again appeared at the Tuberculosis Dispensary after a visit to the country in Virignia. He now weighed 44 pounds, or about the same weight that he had held during the summer of 1912. However, he looked very much better than at any time since spring, and during the fall and winter he improved remarkably. By February 5, 1916, he had gone to 56 pounds and he maintained this weight until June. He felt well and looked well all through the winter of 1915–1916. On November 16, 1915, a first *x*-ray examination of his chest brought out the report that there was infiltration of his entire right lung. Nevertheless, he had no symptoms referable to the lungs and physical signs remained unchanged from those of previous examinations.

With summer, diarrhea and rapid loss of weight again came on. In two months he went down from 56 to 43 pounds; and on August 11, 1916, he again entered the hospital ward for observation and treatment. This time he has diarrhea without pain or tenesmus. It is noted that his bone and glandular disease is no longer active. His abdomen is moderately distended. There is slight but definite diastasis of the recti muscles. There is no tenderness. Deep palpation reveals a small nodular mass just to the left and slightly below the umbilicus. There is no evidence of free fluid, and the liver and spleen are not palpable. It is the impression of the examiner that the history of recurrent attacks of diarrhea together with glandular tuberculosis in other parts of the body and the absence of superficial masses in the abdomen makes the diagnosis of tuberculosis of the mesenteric lymph-nodes (tabes mesenterica) the most probable one. There is probably not a real peritoneal tuberculosis. Another *x*-ray examination of the chest was made at this time, with the report of "marked mediastinitis, infiltration of

both upper lobes, suggesting tuberculosis." The boy left the hospital on August 25, 1916, to go to the country to convalesce.

Three months later he returned to our dispensary weighing 59¾ pounds. He now states that he is feeling quite well, that he is attending school daily, and that he has gained 16 pounds in six weeks. He has lost his pallor and is very well nourished. His abdomen is still distended, with marked diastasis of the recti, while definite masses, from pigeon's egg to hen's egg size, are to be made out in the lower left quadrant. Examination of his chest reveals no change.

He held his ground, although in December, 1916, he began to have a little cough. On January 15, 1917, he was sent to the Maryland State Sanatorium. Here he remained seven months, returning to the dispensary on July 12th. His weight is now 64½ pounds and in every way he shows splendid improvement. He is well nourished and has a good complexion. The scars of his old adenitis are healed. His throat is clear. Over the chest the percussion note is impaired slightly throughout the back and front. There is marked substernal dulness. Breath sounds are harsh front and back, but there are no definite râles. The abdomen shows a most remarkable change since the last examination eight months ago. It is firm, but there are no masses and tenderness.

Thus, after seven months of regulated sanatorium life and eight and a half years since he began coming to the dispensary, the patient, now twelve and a half years old, presents for the first time no symptoms or signs of active tuberculosis. His bone lesions are healed, his glandular enlargements have disappeared, and his abdomen is free from visible or palpable disease. His lungs, which during all these years have exhibited gradually increasing infection, still remain free from manifestations of clinical disease.

During the last eighteen months we have kept in fairly close touch with the boy. Since his return from the State Sanatorium in July, 1917, he has had no recurrence of active tuberculosis anywhere. There are suggestions, however, that the infiltration

of his lungs is slowly increasing. A note made today in the dispensary is as follows: There is slight impairment over the right front to the third rib and throughout the left front. Over both backs there is impairment to the fifth dorsal spine. There is also substernal dulness. The breath sounds are distant over both upper backs. They are vesicular at the bases. No râles are heard even after coughing. The report from the *x*-ray room of an examination made two days ago states that there is infiltration of both upper lobes, especially the right, tuberculous in origin, and marked infiltration of the right base.

Yet this boy stands before you the picture of health. It is true that at fourteen he presents the physique of a boy of ten. Nevertheless, his figure is in good proportion and he looks plump and vigorous. He is unusually bright, stands well in school considering his sadly interrupted schooling, and tells me that he spent last summer and fall traveling through the South with a circus, selling toy balloons, thus helping to support the family at home, and very proud of the fact that he regularly sent back to his mother four dollars a week. He says that he did no hard traveling, that his hours were regular, his food good, and he slept warmly and usually in a tent with plenty of fresh air. Apparently the experience did him no harm.

Here then is a well-looking, very much undersized youngster who almost since birth, his whole life long, has had a battle with tuberculosis. He emerges thus far from the fight with the scars of ulnar, tibial, inguinal, epitrochlear, axillary, and costal abscesses. He has come out the victor over mesenteric gland and perhaps peritoneal tuberculosis. He has kept under control cervical and bronchial gland and pulmonary infection. Time was when he was so sensitive to tuberculin that he reacted locally to $\frac{1}{100000}$ mgm. Just a year ago he failed to react positively to a Pirquet test, and if you will look at his arm today you will see that he again shows no reaction to a Pirquet test applied two days ago. Much information and perhaps several lessons can be drawn from his case; but a discussion of its more striking phases can perhaps be more profitably taken up at this afternoon's clinical lecture.

DISCUSSION OF THE CASE

In considering several features of this unusual and complicated case we shall try to keep sharply distinct, as two separate and not necessarily concomitant conditions, the concepts (1) infection, by which we shall always mean merely localization of tubercle bacilli and the anatomic reaction that may be aroused thereby, and (2) tuberculosis, by which we shall mean a degree of infection or tubercle that has come to the foreground sufficiently to produce noticeable symptoms and signs, in other words, clinical disease demanding treatment. There can, of course, be no tuberculosis without the presence in the body of the bacillus and some form of anatomic reaction to it. But tubercle of varying degree and extent may exist at any particular time without bringing any deviation of an individual's normal health, even though the individual live a normal life, that is, one that can successfully withstand the stresses of life that are common to the individual's age and environment. In such an event the individual is, of course, not ill and should not be looked upon as a sick man, infected though he be with the tubercle bacillus. For the sake of clearness, therefore, we shall restrict the use of the term "tuberculosis" to indicate any condition where there is a lapse from full functional efficiency because of tuberculous infection. Wherever and whenever full functional efficiency exists, though infection may be proved to be present, we shall speak of infection, and not of tuberculosis.

The Onset of the Disease.—Tuberculous infection is our most perfect example of an infection that depends upon intercurrent and accessory experiences on the part of the individual to bring it to light. The number of times that, under the "natural" and more ordinary conditions of infection, primary infection of the human being proceeds and progresses uninterruptedly from initial localization of bacilli to manifest tuberculous disease must be relatively few. All clinical experience and pathologic evidence teach us this. In the vast majority of us primary infection occurs, tubercle in most cases results, and then for a longer or shorter time, perhaps forever, the tubercle remains in abeyance and under the control of the opposing forces of the body, what-

ever these may be. The "balance" that is maintained between infection and the host must, of course, vary in every particular case. On the one hand, the size, the location, the character, etc., of tubercles in individuals will at any given time never be the same. On the other hand, the constitutions of the individuals will be different; their habits and environment will vary just as much; and we at once appreciate that at any given time the reaction of constitution to environment in any two or more individuals can hardly ever be the same. The effect of tubercle on any individual or the effect of an individual's experiences on tubercle must, therefore, in every case be estimated on the basis of the data obtainable—the "merits"—of the particular case under consideration. What may appreciably disturb the "balance" of tubercle and host, what may bring infection into the foreground as tuberculosis, in any one case, may in another be an entirely insufficient force. But with infection once present a situation arises that, theoretically at least, always lays the individual open to an outbreak of tuberculosis. And whether the latter does or does not occur will always depend on whether a determining force is in operation *at a time* that the tubercle is anatomically or physiologically accessible to the force.

Not every woman with tubercle who becomes pregnant and passes through the puerperium develops tuberculosis; but many do. And with most of the latter it is perfectly certain that they would not have fallen ill with tuberculosis had pregnancy not intervened. So far as tuberculosis is concerned, therefore, pregnancy has at this time been the determining event in their lives. Not every child with tubercle becomes sick with tuberculosis after measles or whooping-cough; but a relatively few do; and here again these intercurrent infections have determined the issue. Unusual physical or mental exertion, whether unduly intense or unduly prolonged, not infrequently exercises a similar action; so, very commonly, do a variety of acute infections. In fact, we can generalize, and, using the term in its broadest sense, we can say that "strain" is the great determining factor in the conversion of infection into manifest disease—strain of any kind and of many kinds, which, if sufficient, all end the

same and bring about the same result. This result, broadly speaking, is a disturbance of circulatory relations between the tubercle and surrounding tissue—relations that have heretofore been satisfactory so far as the taking care of the tubercle was concerned. But with an increase and acceleration of circumtubercular physiologic activities we reach a point where the "give and take" between focus and tissue reaches a higher level. Things now are not all so quiet in the neighborhood of the tubercle; and conditions may be established that favor the body's increased absorption of focal products with the consequent production of symptoms, or a change in the character of the tubercle, so that from being a dense, hard, dry and comparatively "lymphless" body it becomes softer, more open and gorged with body fluid, or new channels of dissemination are opened for the bacilli with the consequent better opportunity for extension and multiplication of lesion. The whole matter is assuredly not so simple as I have sketched it; but, whatever else does occur, what I have just told you surely does happen.

Now in our patient's case we find operating toward the outbreak of tuberculosis a factor that is more common than is generally appreciated. This factor is direct trauma. Only two days ago I saw two other patients whose stories are highly significant in this connection. One of them was a young man who was known to have had pulmonary tuberculosis; who had had sanatorium treatment, had been discharged from the institution as an arrested case, and had been working for several months as a chauffeur. While he was starting his automobile the crank flew off and hit him on the left side of the chest. He was at once seized with an extremely sharp internal pain and with dyspnea. On account of the sudden and severe blow he had sustained a spontaneous pneumothorax. Judging from what we have seen of spontaneous pneumothorax at autopsy, we would hazard the guess that what had happened here was the rupture of a thinned-out pleura over a subpleural vomica.

If trauma can thus injure deep-seated tissues when infection is far advanced, there is every reason to believe that it can injure them when lesion is incipient. And as a result we should

expect the same effect that we see following trauma anywhere, that is, an acute inflammation of the injured tissue. If tubercle is present in this tissue, then the result of the acute inflammation in the neighborhood of tubercle would be, under certain circumstances, the same as we have laid down as the effects of strain.

The other patient was a young girl, who to her knowledge had not been ill in years and who had never had any disease except the common infections of childhood. For a year she had been doing unusually heavy work in the car-shops of a railroad and had kept in unusually good physical condition. During an altercation with her mother she was struck on the chest by a broomstick. Two days later, while walking on the street, she was stricken with a pulmonary hemorrhage; and she has been bleeding since and presents the symptoms of acute tuberculosis. Physical and *x*-ray examination bring to light far advanced infection with cavity formation on the side where she was struck—infection that we can think of only in terms of years. Yet until she suffered trauma she was never ill with tuberculosis, and the evidence is almost compelling that the trauma was responsible for the "release" of her tuberculosis.

The influence of trauma, on the production of bone and joint tuberculosis particularly, has, of course, long been recognized and commented upon. It is undoubtedly a very real influence, and the stories that so many mothers tell about the occurrence of a slight injury several days before the manifestation of pain or swelling in a child's bone or joint are by no means stories of merely coincidental events. We must look upon many of them as stories of causative events. Bones and joints are for the most part quite superficial and therefore peculiarly exposed to injury; but they are quite resistant, and if the tissues are healthy at the time of injury the latter's effects soon pass off unless the trauma was a severe one. But if tuberculous infection, quiescent though it may be, is already present, then a relatively slight injury may activate the hidden focus and bring it to the surface.

In his contribution on "Tuberculosis of Children" (Handbuch der Tuberkulose, Brauer, L., Schröder, G., and Blumenfeld, F.,

vol. v, Leipzig, 1915) Hamburger, of Vienna, tells the following story: A seven-year-old boy came to the dispensary with a spina ventosa of the proximal phalanx of the left index-finger. A year before the boy had had a swelling at exactly the same place, but after a few weeks this swelling had healed spontaneously without treatment. Early in January, 1912, the patient jammed his finger at exactly the same place in a door. As a consequence there then developed a slowly increasing swelling, which went on to typical spina ventosa, with the formation of a fistula.

Here again is tuberculosis, following trauma, developing on the site of a previously known though arrested tuberculosis. And if trauma can arouse the quiescent tubercle of what was once but is no longer manifest tuberculosis, then it must be certain that it can activate unsuspected tubercle that has never before reached the stage of manifest disease.

Site of First Infection.—This boy's first infection certainly was not at the site where tuberculosis first manifested itself. It is inconceivable that the ulna and the tibia were the first resting places of tubercle bacilli in his body. These must have come from some pre-existing focus or foci; and it may be profitable for us to discuss the probabilities in this case with their relations to the matter of first infection in general.

And, as introductory to this discussion, we may for a few moments consider the matter of the probable time of first infection. Taking tuberculosis in the large, there is, as a rule, no more difficult and treacherous task in clinical practice than to try to determine when infection first occurred. Even in the child, unless it be a very young infant or one who has been under continuous observation, and has been periodically tested for infection, hardly an approximation to the truth is possible. In the adult, of course, the question is ordinarily altogether incapable of being answered. For the clinician there is no incubation period—the time between an infection and the outbreak of disease—for tuberculosis. Conceivably it may be days or weeks. Perhaps it is months. But undoubtedly it very frequently, and perhaps usually, is years. In most human beings the incubation

period never runs out; most people go to their graves from other causes, and in them tuberculosis never develops from infection.

Nevertheless, as compared with the adult, a child's activities and biography have been relatively simple and clear-cut, and opportunity now and then is given us to make some kind of a passably correct guess as to the time of first infection. Subsidiary data, matters of past history, are now important and help much.

In this particular child's case the history gives us one hint and only one. This is that his twin sister died at the age of one year of "mumps." Now, just what was this "mumps"? We certainly will not accept the diagnosis or statement of the mother without absolute verification. Mumps at the age of one year is an extremely rare affection, even though an infant be exposed to the disease. Death from mumps is perhaps still more unusual. Now mumps is a disease of which the visible evidences are tumors in the region of the mandible and neck. There are two vastly more common affections which might attack young children and which to the uninformed may give neck manifestations that may be confused with mumps. By far the most frequent cause of swellings in the neck in infancy and childhood is cervical tuberculous lymphadenitis. A more uncommon similar condition is that due to severe pharyngeal diphtheria; but it can and does occur. Yet, if this boy's twin sister had had fatal diphtheria, we should expect some history of the boy also having had the disease. Indeed, unless the contrary can be shown, every probability indicates that the sister had a tuberculous lymphadenitis that eventuated in meningitis and death.

Were this the case, then it would be more than likely that the patient received his initial infection at about the same time as his twin sister, that is, at the age of one year or before.

Where was this first infection? Again we cannot answer with absolute certainty, but it seems to me that we can arrive at a fairly satisfactory conclusion.

When this boy first came to the dispensary in 1909 at the age of four years it was already noticed that things were not en-

tirely right with his abdomen. A note was then made that it was distended. Of course, it is entirely possible that this distention was nothing more than the pot-belly of rickets. Be this as it may, we read a year later that a mass is palpable in the region of his descending colon. And all through his history there is an occasional recurrent note of possible trouble in his abdomen. He finally, after six years, in 1915 becomes a case of tuberculous peritonitis. And in the next year we have the record of one examiner who is definitely impressed by the probability that this peritonitis is really a matter of tuberculosis of the mesenteric lymph-nodes.

Meanwhile, during the first two or three years all examiners agree that the throat, neck, and lungs are "clear," except when an acute infection of the throat occurs.

Under ordinary curcumstances there are two, and only two, major portals of entry of the tubercle bacillus. These are the nose and mouth. Taken in by ingestion, bacilli can originate primary infection in structures that are tributary to the digestive tract at several points—cervical lymph-nodes, tonsils, and mesenteric nodes. Inhaled superficially, they can set up infection in the cervical lymph-nodes; and inhaled deeply, it is very likely true that they can arouse foci in the lungs and their tributary nodes, the tracheobronchials. Bacilli can go by way of the circulation from mesenteric nodes to lungs; but it would be impossible to get from lungs to mesenteric nodes in any considerable number by the same route. If lungs were involved, and if, as a consequence, ulceration occurred, bacilli might get to mesenteric nodes from sputum that had been swallowed; but from 1909 to date there is not the least suggestion that this sequence of events has occurred. The situation that here confronts us is one where originally the entire respiratory tract and the upper part of the digestive tract are free from visible infection, while the lower part of the alimentary canal exhibits infection that has progressed as far as manifest disease. Under the circumstances no clinical case can be clearer than this. We are almost undoubtedly dealing with a case of primary alimentary infection in which the micro-organisms have got by the intestines

and have been carried to the tributary mesenteric nodes, there to set up infection. And always remember that, unless ulcerative lung disease can be proved to have preceded it, every infection in nodes that immediately drain any part of the digestive tract must always be classed as having come from the outside and as being in this sense primary. The same cannot be said of pulmonary tuberculous infection. The lungs are the converging point of foreign particles that start from any part of the periphery of the body and thence make their way to the afferent circulation.

I think it established almost beyond dispute that we are here dealing with an instance of primary alimentary infection—feeding infection. And we desire more than ever to know more about the infant history of this boy and his sister. Is it possible that the twins were fed tuberculous milk, and that the sister early developed cervical lymphadenitis and meningitis, while the patient began his tuberculous career with infection of the intestinal lymph-nodes, brought about by the same cause?

The Etiology of the Infection.—A primary tuberculous infection of the lower alimentary tract in an infant or child is presumptively of bovine origin. Hand-to-mouth transmission may and frequently does give rise to primary human infection of the upper digestive tract—cervical lymphadenitis. But it is questionable whether it commonly initiates first infection from the intestines. Acted upon by the digestive juices, buried in feces, hurried along by the movements of the alimentary canal, intestinal infection demands that unusually large numbers of bacilli are ingested, and, in the absence of ulcerative pulmonary lesion, this condition does not commonly obtain unless the large numbers are taken in with food. It would be rare to have food thus grossly contaminated with bacilli from human sources. Experience has shown that the milk of tuberculous cows fulfils these conditions.

In the present instance the course of events bears out the presumption. In the human being manifest bovine tuberculosis is, with excessively few exceptions, non-pulmonary, no matter how wide-spread it may become. It may spread from point to

point, and in time succeed in involving a number of tissues of the body. It may get to the central nervous system and eventuate fatally as meningitis. But manifest—*symptomatic*—pulmonary tuberculosis of bovine origin is almost a medical curiosity.

Pulmonary *infection?*—yes. During the last ten years we have seen detectable infection of the lungs in this boy develop and gradually extend. His first examinations failed to bring out lung involvement. Six years later according to the *x*-ray report there was "infiltration of the entire right lung." Two days ago the *x*-ray reveals "infiltration of both upper lobes, especially the right, tuberculous in origin, and marked infiltration of the right base." Meanwhile physical examination has kept pace with *x*-ray pictures; or, vice versa, as you choose. The fact remains, the point to be brought out is, that infection of the lung is so slow, so creeping, so benign—we do not know enough to use more accurate terms—that it does not bring about the clinical picture of pulmonary tuberculosis. And this is the customary event when the bovine tubercle bacillus becomes engrafted on man.

The case is quite similar when we infect cattle with the human bacillus. Personally I have but an extremely limited experience with experimental inoculation of cattle. But I have followed a few cows that received large intravenous doses of human bacilli. In none did I ever see progressive pulmonary lesion characterized by much necrosis and degeneration of tissue develop. Whatever pulmonary lesion was set up tended to heal. Meanwhile there occurred an occasional abscess in a bone or joint, or foci in lymphatic nodes that sometimes went on to caseation. Experimental veterinarians have told me that their experience has been similar—that it is not the "genius" of the human tubercle bacillus to bring about degenerative, and therefore progressive, lesion in the lungs of cattle. Why this is I do not know; nor will time permit a present discussion of probabilities.

All in all, I am inclined to believe that the boy became infected first in infancy, that the bovine bacillus was the etiologic factor, and that primary infection was alimentary, involving

the mesenteric lymph-nodes. And I also again hazard the guess that his sister developed cervical adenitis from the same cause and that she died of a metastatic tuberculous meningitis.

The March or Progression of Infection and Disease.—With the site of primary infection settled to our satisfaction, it now becomes a fascinating exercise to speculate concerning the subsequent transportation of tubercle bacilli throughout the body. Here complexity begins and grows apace. And if it does nothing else, the case should illustrate to you the enormously varied possibilities and multiplied chances of localization once microorganisms escape from a localized focus that is tributary to the portal of entry.

To get from a primary focus like the mesenteric lymph-nodes or directly from a portal of entry like the intestines to the ulna and tibia the bacilli had to make practically the entire circuit of the circulation. At first the journey was centralward, centripetal, by way of lymphatics to thoracic duct, thence to the venous system, then through the right heart and lungs, then peripheral and centrifugalward through the left heart to be distributed by the arterial system. Localization in peripheral bones occurs; but how long before the onset of symptoms of tuberculosis we can only speculate. All we know is that by January, 1909, manifest tuberculosis of ulna and tibia was established.

Almost a year goes by before we next hear of the recurrence of manifest tuberculosis in other places. This time disease manifests itself in locations that are central to, but directly in the path of drainage of, the areas of primary disease—the left cubital and the right inguinal nodes. The transmission of bacilli is again centripetal by way of the lymphatics. But we cannot believe that it took a year for the bacilli to make the short journey from ulna to epitrochlear nodes and from tibia to inguinal nodes. As to what really happened we can judge only by what we learn from controlled, experimental observations; and here we usually see the transportation from original focus to tributary lymph-node taking place within a few days. Given the focalization of tubercle bacilli in tissues in any particular

place, their appearance in or, in other words, infection of regionary nodes always rapidly follows. But manifest tuberculosis of the nodes is another matter—this may take weeks or months.

I have lately found that after subcutaneous inoculation tubercle bacilli will proceed from the right groin of guinea-pigs to the tracheobronchial nodes in four days and perhaps earlier. This means that in this time the bacilli, introduced into the domain of the lymphatic system, have passed all barriers, such as the superficial and deep inguinal nodes and the iliac and aortic nodes, and have thence proceeded to receptaculum chyli, thoracic duct and subclavian vein, when the passage by way of the blood through right heart and lungs to the tracheobronchials was relatively unobstructed. This I was able to prove by the inoculation of tracheobronchial nodes into normal guinea-pigs. But I have not seen histologic tubercle in these nodes earlier than about eighteen days, while gross tubercle is not, as a rule, ascertainable before the lapse of a month.

Everything else being equal, it is dosage of infecting tubercle bacilli that largely determines the rapidity and degree of lesion arising at any particular point—and, besides the numbers that may be carried to a spot, by dosage we also include the multiplication of bacilli that might there occur. When dosage becomes sufficient, manifest lesion, or tuberculosis, will result. So long as it remains insufficient, then infection without manifest lesion may continue for a long time—undoubtedly for years. The term "sufficient" means enough at any particular time, for it is self-evident that, if we gratuitously assume the potentialities of the bacillus to represent a constant, then the fluctuating reactions of a variable like the body will largely determine the issue of infection.

But if we marvel at the lazy development of tuberculosis in the epitrochlear and inguinal nodes after its first appearance in the ulna and the tibia, what shall we say about its first real manifestation in the left axillary nodes? This did not become symptomatically apparent until four years had gone by since epitrochlear disease was first noted. Progression is still centralward by lymphatics; and it takes manifest disease four years

to leap the short gap between epitrochlear and axillary nodes. Yet it is significant that in April, 1911, sixteen months after the appearance of epitrochlear disease and almost three years before the first manifestation of axillary tuberculosis, there is a note that the left axillary node is just palpable.

You will never get a better opportunity to observe in a human being this characteristic behavior of tubercle that I have been so insistent about all through this talk, namely, the prolonged subsidence yet continuance of infection without the manifestation of clinical tuberculosis. This case develops under our eyes and is plain. Most cases we get only occasional glimpses of and are not so clear; but the net and sifted result of all clinical, pathologic, and experimental data continually teaches us that what we are now considering is the normal course of tuberculous infection. We cure, we heal tuberculosis when we have forced it into the obscure background, but as for wiping out infection by our present methods of therapy, that is another matter and one that no man can be certain of.

A feature of this boy's case that has always interested me is the swelling of his legs that was complained of and noticed at his first visit and which afterward elicited occasional comment. What was it due to? Was it simply an edema consequent to the inflammatory lesion of his leg bones? Against this explanation is the fact that it was bilateral. There is nothing to direct us to a disturbance of the kidneys or the cardiovascular system for the cause. Perhaps it was due to his anemia, although later, when his hemoglobin ranged from 50 to 60 and when his constitutional condition was apparently not so good, the swelling of the legs had disappeared.

We must consider the possibility of this swelling being due to some intra-abdominal lesion. It is surely conceivable that by the time the boy first came to the dispensary bacilli had drained from his tibial lesion, past his inguinal nodes, to his retroperitoneal nodes, or from his mesenteric nodes to the latter, or that a transmission from both sources to the retroperitoneals had occurred, and had here set up a lesion sufficient to bring about slight obstruction to the venous circulation of the lower

extremities. I merely throw this out as a guess and with the purpose of directing your attention to the importance of investigating every single abnormality when a diagnosis is to be reached. Unfortunately, we have no record that any attempt was made to explain the swelling of the legs.

Peripherally and centralward, centrifugally and centripetally, in both directions at the same time, infection was proceeding. Grasp this fact and you will at once appreciate how enormously complex are the factors of tuberculous infection. Proceeding centralward by lymphatics the bacilli tended to converge and dosage accumulated; and, therefore, manifest lesion was more likely to result. Scattered peripheralward by the arterial system, the tendency was to a wide-spread distribution of bacilli, and, therefore, to a localization in small dosage with factors working against the production of manifest tuberculosis. Therefore, after the first manifestation of peripheral tuberculosis we meet with it no more; afterward the tendency is always to more and more central focalization.

And through it all, so far as our examination of the living patient will permit, as time goes on we meet with a heaping up of infection in the lungs and tracheobronchial nodes, the ultimate converging points of foreign particles that journey from periphery to center by way of the circulation. Why symptomatic tuberculosis has never appeared in the lungs we have already discussed.

Treatment.—If this case teaches you nothing else, it should forever impress upon you the transcendent importance and value of change from ordinary environment and of sanatorium care in the therapy of tuberculosis.

You have had an unusual opportunity to observe what mercury and iodids will do in a case of tuberculosis. Both are among the thousands of drugs that have been brought forward to combat this disease. Both did nothing so far as we can observe; both were no better and no worse than most other remedies that are not pushed to the point of specific injury to the patient.

Again, you have heard this case through what is almost a unique course of tuberculin therapy. In the tuberculosis dispensary at that time hope reigned eternal and Koch's remedy

was not discontinued until over five years had passed by. In fact, it was not given up until frank peritonitis or tabes mesenterica had become so obtrusive that it could not be disregarded. In this particular case one would be hard put to it to prove that tuberculin had benefited the patient.

Now a word as to tuberculin in the therapy of tuberculosis.

No question is more commonly put to us who spend our time in tuberculosis laboratories than the one, "Does tuberculin have any action on tuberculosis?" Our only answer can be, "It most certainly does." Nothing is easier for us to demonstrate scientifically than the action of tuberculin on tubercle. If we inject a tuberculous guinea-pig with a sufficient dose of tuberculin we will bring about the animal's death, and at autopsy we will find the periphery of the tubercles in a condition of acute inflammation—of focal reaction. This effect most decidedly represents an action of tuberculin on tubercle.

Or let us make the case simpler and from beginning to end more visible.

By inoculating with living tubercle bacilli the anterior chamber of a rabbit's eye we bring about the production of localized tubercle. If, after this has developed, we inject the animal with tuberculin intravenously, within an hour or two we find that an acute inflammation—a focal reaction—is being set up around the tubercle. Within a day or two this reaction subsides and conditions return to what they were before the injection of tuberculin. But now, as a direct consequence of this reaction, a very remarkable and significant thing happens. Within a few weeks this "reacted" tubercle disappears. The eyes of control rabbits that have not received tuberculin go on to panophthalmitis and destruction. And we have long been in the habit of affirming that nothing is more certain than that *in localized tuberculosis of a certain type* tuberculin by focal reaction can bring about the disappearance of tubercle.

Now, tuberculosis, as it usually presents itself to us in man, is hardly ever so simple a matter as is a small, isolated focus in a rabbit's eye. It is a much more massive combination of pathologic processes in various states of development. Consider, for

instance, the common type of pulmonary involvement that we designate as chronic apical infiltration. We have to do here not with one tubercle, but with several or many, every one of which may be in a different state of pathologic development. The various foci all differ in their degree of accessibility to the tuberculin, for some may be well encapsulated by scar tissue, while others may be quite soft and be only slightly invested. We know, too, that tubercles of different anatomic types will react differently to tuberculin, even though the dosage applied to each is the same, and that it takes much more tuberculin to react old, fibrous tubercle than progressive, cheesy foci. With the latter type of focus too the tuberculin may react quite disadvantageously, for the result may be a more rapid breaking down of tissue and consequent dissemination of the tuberculous process. This multiplicity of both number and type of lesion is why tuberculin is of such limited service in the therapy of pulmonary tuberculosis.

The case of this boy was more or less similar to what we have just been discussing. He had multiple tuberculosis brought about by foci of different ages and anatomic types. As a rule these ran a chronic course, but sometimes they became more acute. Under the circumstances it would be perfectly impossible for us to control and regulate our dosage of tuberculin so that all foci would be acted upon equally favorably. Indeed, it is more than likely that even though we might be influencing one or another focus for good, we might be doing harm to others. This, it seems to me, is the reason why such poor results were obtained with tuberculin in this particular case.

The matter of administering tuberculin therapeutically should always be determined by the merits of every particular case. But I think I can lay down a few generalizations which may help you, and some of which, especially the first, I hope you will remember.

First, tuberculin should never be given therapeutically except under the direction of an expert—of one who has had the widest experience in its use.

Second, it should never be used in acute tuberculosis; and

its use is questionable in chronic cases in which the maximum daily temperature is showing a tendency to exceed 100° F.

Third, it may be used in chronic cases, but even then only with the greatest discretion.

Fourth, before it has been given a fair trial, no one can predict which case will or will not do well under tuberculin. Therefore, as in every other disease, never make a definite prognosis until you have based this on sufficient observation of the effects of treatment.

Fifth, the case of tuberculosis *par excellence* for tuberculin therapy is the afebrile, chronic type. Slight elevation of temperature is no bar to its use.

Sixth, tuberculin in therapy, as it has been indiscriminately employed, has done much harm.

Seventh, it has, on the other hand, undoubtedly had to its credit victories that are more striking than can be ascribed to the use of any other form of treatment.

Eighth, its results are often little short of remarkable when the disease is localized and superficial; in other words, where its action can be watched. This makes it an invaluable agent in treating eye and skin tuberculosis, provided there is at the same time no lung involvement.

Ninth, tuberculosis is eminently a disease of "ups and downs." Therefore do not ascribe every favorable turn of events to tuberculin unless you can prove your case; and, as a corollary, do not discontinue its use upon the least sign of "slipping" on the part of the patient.

Tenth, if a constitutional reaction occurs during the course of treatment, it is a sign that the focus has reacted. Therefore "rest" the patient from tuberculin for at least two weeks; and, if signs and symptoms of increased focal activity continue, then until these have subsided.

But, if antisyphilitic treatment and tuberculin therapy did this boy no good, life away from home in the country and sanatorium regimen surely did. He was first sent to the country in the summer of 1913, and although it had been his habit to lose weight in summer, he returned weighing $3\frac{1}{2}$ pounds more

after a sojourn of six weeks. In the spring and summer of 1915 his abdominal symptoms were making themselves felt and for two months he lay in bed in the hospital, meanwhile going down hill steadily. Discharged in July, he went to the country, and returned to town in September much improved. The next summer, in 1916, he again began to have diarrhea and failed appreciably. After a short stay in the hospital he again went to the country, and came back with the amazing story that he had there gained 16 pounds in six weeks. And this was the real beginning of his "cure."

He went to the sanatorium in January, 1917, and remained there seven months. When he came back he was a different boy. His abdomen showed no signs of disease. Masses that had been palpable for seven years had disappeared. The scars of his old adenitis had healed. He was now well nourished and had a good complexion. For his height his weight was above normal. "Splendid improvement" is the note the examiner made. And since his return from the sanatorium he has not retrogressed. His "cure" has thus far been permanent, and meanwhile he has lived the normal life of a boy of his age and more.

Sanatorium treatment means a great many things. It means regulation and discipline; regulation of rest and exercise, of diet, and of life in the open. But, above all, it means relief from strain. Just as it is strain that brings infection up above the surface as tuberculosis, so it is relief from strain that allows tuberculosis to subside into quiescent infection. Strain and its effects are relative matters; and where and when shall we say that strain begins to exhibit itself? This question may often be hard to answer, but probably our best criterion is to designate as strain any exertion that brings about symptoms of fatigue in the patient. Here again you see we must pass judgment on causes after observing effects in the individual patients; for it is obvious that what will fatigue one patient may be thoroughly well borne by another. And remember, please, that to some there is no fatigue that is quite so exhausting as being bored—*ennui* may wreck as many lives as overexertion.

At any rate, in our treatment of tuberculosis, next to keeping up the nutrition of the patient—and, as a rule, this will take care of itself, provided food is at hand and digestion is functioning properly—our whole effort should be directed toward preventing fatigue—weariness—weariness of mind as well as of body. And the amount of rest and exercise to be prescribed for any particular patient will be regulated by the patient's reaction. Either may be little or much; but either must stop short of bringing about physical fatigue or boredom.

We have our advocates of sanatorium treatment and our exponents of home treatment. Both are sometimes equally ardent, passionate, and strident. As a matter of fact, tuberculosis can be arrested at home just as it can be in the sanatorium; on the coast of Norway, in the Arizona desert, in the cool and cloudy Adirondacks, or in the smoky atmosphere of Pittsburgh. There is no doubt that both the home-treatment advocate and the sanatorium-treatment advocate could exhibit in court equally imposing and striking arrays of patients to substantiate his claims. Yet there can be just as little doubt that for most of us who can get it, sanatorium care is best. The crux of the argument is and always will be the matter of discipline and relief from petty care and strain. And surely no one will quarrel with the statement that both these all-important requirements obtain to a vastly larger degree in well-regulated sanatoria than is usually possible at home. The sensible, co-operative patient who has tried both forms of treatment has only one answer—invariably he is for the sanatorium.

The Pirquet Skin Test.—After the waste of a precious year, after a course of antisyphilitic treatment, during all this time this patient was at last found to be tuberculous by the way in which he reacted to the Pirquet test. This is one of the most significant features of his case, and one that should leave a strong impression on you.

By this time you have seen the test applied sufficiently often for you to have formed some judgment of its meaning and its range of usefulness. You have seen perfectly healthy children in whom there is not the least manifestation of tuberculosis

react positively. You have seen other healthy children fail to react. You have seen children in whom there are undoubted symptoms and signs of tuberculosis react positively. The test is a test of *infection*. A positive reaction tells you merely that tubercle is present in the body of the reactor. It tells you nothing concerning the latency or the activity of the infection. The usefulness of the test, therefore, is greatly limited in clinical practice. Nevertheless, the present is a case in which the test was of great service. We have come to say that a positive test in a young child or a negative test in an adult is significant. This means that when we employ the test diagnostically the clinical condition before us is obscure; and if, under these circumstances, a young child reacts positively we are justified in presuming that the case is one of tuberculosis; while if an adult reacts negatively the disease is something else.

We must again hedge this statement with certain qualifications. In general, acute infections and any highly febrile condition operate toward inhibiting a positive reaction, even in a known reactor. This inhibition is particularly striking during the acute stage of measles. We also find the reaction more or less blunted (even to the point of disappearance) when a chronic case of tuberculosis becomes acute. Therefore we must not lay too much stress on the significance of a negative result if the test is applied during the time that a patient has high fever or another acute disease. In tuberculous meningitis, too, the test often fails us; and now and again this is a condition that may be most difficult of diagnosis. The same may be said of miliary tuberculosis, that hardest of all diseases to diagnose when it occurs in an adult who has previously been in health and has not been known ever to have had tuberculosis.

However, do not let all this lead you to abolish the practice of this simple test. It will often give you just the information you want. With an adult before you it will now and again straighten you out as between chronic pulmonary tuberculosis and bronchiectasis, or between tuberculosis and malignant tumor, or tuberculosis and syphilis. Active tuberculosis without much fever should practically always react positively; and if the

test is negative you can rule out this possibility. Chronic and obscure conditions in childhood, in which blood examination yields no information and a Wassermann test is negative and a Pirquet test is promptly positive, are in the vast majority of cases tuberculosis.

No biologic test in medicine is more simple—a puncture of the epidermis of the flexor surface of the forearm through a drop of old tuberculin. Let the tuberculin dry before dismissing the patient. "Read" the test at one, two, and sometimes three days after it has been applied. An area of redness and papule formation of over 5 mm. in diameter or a papule without redness of the same size or persisting redness without papule formation over 10 mm. means a positive reaction. If you make a control scarification, see that you do this at a point distal to the application of tuberculin; and in replacing the patient's sleeve see to it that no tuberculin is carried down from the tuberculin scratch to the control scratch.

All the possibilities of this test are probably little short of enormous. It not only can be a very valuable aid in arriving at a diagnosis of baffling conditions that defy our most elaborate methods of examination. It can also be applied to epidemiologic studies of tuberculous infection on the largest possible scale, and this with but slight inconvenience to the person tested and with but little trouble and preparation on the part of the tester. Localized studies of the incidence of tuberculous infection have been made with this test, but we await the day when it will be applied to large numbers of our population and thus give us data that is more beyond critical attack than any that we now possess.

While it is true that every positive reaction to the Pirquet test means tuberculous infection, it is not so certain that every failure to react means the absence of infection. We have already seen that certain intercurrent infections and high fever tend to diminish or even abolish the reacting capacity of an individual. But over and above these cases, there are a certain number of people, the proportion of whom is relatively small, who at times fail to react to the test, even though at the time they undoubtedly harbor tubercle and at the same time are in health.

Our patient is a case in point. He is not free from infection. Physical and *x*-ray examination of his chest would at once demonstrate this fact. Yet during the last two years he has failed to react. How shall we explain this?

Cutaneous hypersensitiveness to tuberculin is a fluctuating affair. I have had the opportunity to observe this experimentally (Journal of Medical Research, 1916, xxxvi, 1). As tuberculous infection is established, it becomes manifest. As infection develops, it increases; but as infection comes more and more under control, it diminishes. If at any time reinfection occurs, it again increases rapidly and to a high degree. But even though infection may become so limited that it almost reaches the vanishing point, a hypersensitiveness of some degree persists. This may be very slight and require more than the ordinary dose of tuberculin to elicit it; but some slight degree is always present so long as there is any infection.

Any and every person with tuberculous infection can be made to react to tuberculin; but it may be that the amount of tuberculin required is more than is absorbed when the ordinary Pirquet test is performed. I have no doubt that I could obtain a positive reaction in this boy if I applied enough tuberculin to his skin or injected enough intradermically. He fails to react now to an ordinary Pirquet test because his infection is so well healed—so well, but not completely. But the application, the absorption of more tuberculin would surely cause him to react sooner or later.

At any rate, I would repeat that while a positive Pirquet reaction makes tuberculous infection absolutely certain, a negative reaction does not rule out the presence of infection. Every tuberculous animal and person can be made to react if given enough tuberculin. As a rule, in human beings, the amount applied in a Pirquet test is enough. But it sometimes happens that it is not, and then we must resort to methods that assure better absorption of tuberculin, such as intradermic and subcutaneous applications.

One more word before leaving this subject. When making tests always be sure that your tuberculin is active and potent.

Experience has taught us that occasionally the proprietary preparations are inert. Too continuous and large a series of negatively reacting patients should arouse your suspicions, which can easily be verified or dismissed by testing a known reactor with the substance.

Prognosis.—So far as prognosis is concerned, this boy's case illustrates the rule that we have found to hold good for tuberculosis in childhood. Unless generalized miliary tuberculosis and meningitis supervene, the prognosis is extraordinarily favorable. As your acquaintance with tuberculosis grows older you will surely be more than once astonished at how much tuberculous involvement can be recovered from by children. At this age the tendency is for infection to accumulate and become manifest in places other than the lungs; and although scarring and deformity may result, death is much less frequently a terminal event than is the case with manifest tuberculosis in the adult. You are therefore justified in being quite hopeful as to the immediate outcome; yet you should always safeguard yourself with one or two reservations, namely, that generalized miliary or meningeal tuberculosis may be ever imminent.

It will be unusually interesting and instructive to keep watch over this boy from this time on. He is now approaching adolescence, the age when pulmonary tuberculosis tends to develop. We know that he now has pulmonary infection, and apparently a great deal of it. And we may learn much by observing how he reacts to the physiologic and economic strain of the life that he will soon enter upon.

General Summary.—Whatever we may have learned by the way in our consideration of this case, I want you to take away with you the picture of a perfectly healthy though much undersized boy who during practically his whole life has had active tuberculosis in many places in the body, who once was so sensitive to tuberculin that he reacted to $\frac{1}{100000}$ mgm., but who for the past two years has failed to react to the Pirquet test. His disease began with trauma. Its onset was so obscure as to be diagnosed syphilis. It was detected by the Pirquet test. It was finally arrested by life out of doors and sanatorium treatment.

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